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ii, 668	16	"Grignard" read "Guignard."

\* From bottom.

JOURNAL  
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TRANSACTIONS.

*The Activity of Acids as Catalysts in Relation to the Nature of the Solvent Medium.*

By HARRY MEDFORTH DAWSON.

In previous investigation (Dawson and Wheatley, Trans., 1910, 2048) of the relative rates of tautomeric change of various ketones, in which iodine was used as an indicator of the speed of reaction, the choice of a solvent for the reacting substances was determined by a preliminary examination of the variation of the rate of change of acetone when the water serving as solvent was usually replaced by ethyl alcohol. In these experiments, which were made at a temperature of 20°, the concentrations of the acetone and of the sulphuric acid, which was added as a catalyst, were increased to the same extent, the experimental data thus indicating directly changes which are attributable to the variation in the character of the solvent medium. The concentrations of the ketone and the acid were, moreover, such that the active mass of the former remained practically constant during the change, whilst the effect of the latter was not altered to any great extent by the hydroiodic acid formed as one of the products of the reaction. With increasing concentration of ethyl alcohol in the solvent, the reaction proceeds less rapidly, but the mechanism of the change is apparently unaltered, for the iodine disappears at a constant speed so long as the amount of iodine present is appreciably in excess of that

corresponding with the state of equilibrium which is ultimately attained.

The dependence of the reaction-velocity on the composition of aqueous alcoholic solution is shown by the data in table I, in which it is seen that the velocity is practically the same in water-alcohol mixtures as in pure water, provided that the amount of water present does not fall below about thirty volumes per cent. On further diminution of the water content of the solvent the velocity increases, and the rate of increase becomes greater as the amount of water present is continuously diminished. The values of  $k = dx/dt$  are expressed in mols. per litre per minute.

TABLE I.  
Acetone, 0·272; Sulphuric Acid, 0·05 mol. per litre.

Grams water per litre of solution	1000	800	600	500	400	300	200	119	48·5
$k \times 10^3$ .....	23·0	23·0	22·5	22·5	22·0	24·0	25·5	32·0	63

On account of the high speed of the reaction, measurements could not be made with sufficient accuracy at 20° in the cases of solutions containing less than about one gram-mol. of water per litre, and the investigation of these was carried out at 0°. In these determinations anhydrous alcohol was prepared by Wini's method (*Ber.*, 1905, **38**, 3612), the material used in the preparation of the anhydrous and moist alcoholic solutions being the product obtained after triple treatment with rasped calcium.

With this anhydrous alcohol, a solution was prepared containing 0·05 mol. of sulphuric acid and approximately 0·05 mol. of acetone per litre. Fifty c.c. of this were introduced into stoppered bottles containing weighed quantities of water, and the volume made up to 100 c.c. with anhydrous alcohol; these solutions were then heated to 0°, and 2 c.c. of acetone were added to each. Measured volumes of the solutions were then removed from time to time, and the unchanged iodine was titrated, as previously described.

In order to show the course of the reaction in its earlier stages in alcoholic solutions containing little or no water, two experiments are recorded in detail in table II. The measured iodine concentrations in mols. per litre are given under  $x_1$ , and the values calculated from  $x_2 = x_0 - kt$  under  $x_2$ .

TABLE II.  
(1) Anhydrous Alcohol.

Time (minutes).....	0	15 <sup>a</sup>	23	30	3
$x_1 \times 10^3$ .....	22·45	19·83	18·14	16·90	15
$x_2 \times 10^3$ .....	(22·45)	19·51	18·08	16·75	15
$k \times 10^6$ .....					

<sup>a</sup> 0·00019.

## (2) Alcohol containing 5·02 grams of water per litre.

Time (minutes) .....	0	20	50	80	110	150
$\frac{1}{2} \times 10^3$ .....	22·23	21·39	20·32	18·98	17·37	15·54
$\frac{1}{2} \times 10^3$ .....	(22·23)	21·37	20·08	18·79	17·59	15·78
$k = 0\cdot000018$ .						

These data suffice to show that the rate of disappearance of the ion in anhydrous alcohol and in alcohol containing a small quantity of water is constant, as was previously found for aqueous ions under similar conditions. From this it seems justifiable to conclude that the mechanism of the reaction under investigation is the same. In table III are given the reaction velocities observed in two series of experiments exactly similar to those recorded in table II. The solutions were made up as already described.

TABLE III.

## Series 1.

## Series 2.

Grams of water per litre.	$k \times 10^3$ .	Grams of water per litre.	$k \times 10^3$ .
0·0	190	0·0	192
5·0	43	5·1	45
10·1	21	10·0	22
20·0	9	20·1	9

In two series of experiments were quite independent, different types of anhydrous alcohol being used in the preparation of the sets of solutions. It is evident that a small quantity of water increases the speed of the reaction to an enormous extent, the velocity being about one tenth of its value for anhydrous alcohol on the addition of 1 per cent. by volume of water. In view of the slowness of the speed of the reaction towards traces of water, the agreement between the two values for anhydrous alcohol is remarkably good, and affords some guarantee that the alcohol used by Winkler's method was really free from water. The data are not sufficient to show the exact connexion between speed of the reaction and the water content of the alcoholic ion, but it is evident that for solutions containing from 5 to 20 grams of water per litre, the velocity is approximately inversely proportional to the amount of water present.

The fact that small quantities of water exert a considerable lessening effect on the velocity of chemical change in alcoholic ion is well known, and appears to have been first observed by Schmidt in connexion with the process of esterification (*Ber.*, **28**, 3218; 1896, **29**, 2208; compare also Goldschmidt and Uhlmann, *ibid.*, 1906, **39**, 711; Goldschmidt and Udby, *Zeitsch.*

*physikal. Chem.*, 1907, **60**, 728; Wegscheider, *Ber.*, 1906, **39**, 1 Kailan, *Monatsh.*, 1906, **27**, 543 *et seq.*). Other reactions to place under the influence of acid catalysts are similarly affected was found by Bredig and Fraenkel (*Ber.*, 1906, **39**, 1756) in case of the decomposition of diazoacetic ester in ethyl-alco solution, by Tubandt and Mohs (*Annalen*, 1907, **354**, 259) in inversion of *l*-menthone in methyl-, ethyl-, and propyl-alco solutions, and by Lapworth and his co-workers (Lapworth Fitzgerald, *Trans.*, 1908, **93**, 2163; Lapworth, *ibid.*, 2187; Lapw and Partington, *ibid.*, 1910, **97**, 19) in the conversion of hyd benzene into benzidine, the action of bromine on ketones, and hydrolysis of esters in non-aqueous media. The rate of de position of oxalic acid by sulphuric acid was also found by Bi and Lichty (*Zeitsch. Elektrochem.*, 1906, **12**, 459) to be very retarded by small amounts of water in excess of that correspond with the composition  $H_2SO_4$ .

Of these various catalysed reactions, the one for which influence of water has been examined in greatest detail is the pro of esterification in ethyl-alcoholic solution. In regard to influence of small quantities of water on the velocity of keto- $\rightarrow$  transformation a few preliminary measurements only have made in the case of acetone without added solvent in presence sulphuric acid as catalyst and bromine as indicator (Lapw *loc. cit.*, p. 2189).

In the case of the experiments described in this paper, the range of alcohol-water mixtures has been examined. To facilitate the comparison of the data obtained at 20° for solutions containing larger quantities of water (table I) with those obtained at solvents containing relatively little water or none at all (table II) the velocity of the reaction for the solution containing 18.5 g<sup>1</sup> of water per litre was measured at both temperatures. The of the reaction was found to be reduced from  $k = 170 \times 10^{-6}$  at 20° to  $k = 13.5 \times 10^{-6}$  at 0°. Assuming that the temperature coefficient has the same value for a water-free alcoholic solv and taking into account the small difference between the acid concentrations in the two series of experiments, it is found that velocity of the reaction in anhydrous alcohol is more than a hundred times (about 115) as great as the velocity in aqueous solution.

The data in table II show that this enormous difference in rates of change in the two media is not accompanied by observable difference in the mechanism of the change, for both aqueous and in alcoholic solution the speed of the reaction independent of the iodine concentration. The change in velocity is therefore attributable to a difference in the rate of the pri

meric change in the two media, and since this change is typically accelerated by acids, the difference in question may be to a change in the specific reactivity of the acetone or to an alteration in the catalytic activity of the acid.

reference to this change in activity, experiments were made to determine the influence of the acetone and acid concentrations on the velocity of the reaction in nearly pure alcoholic solutions, whose measurements (Dawson and Leslie, Trans., 1909, **95**, 1860) have shown that the velocity in aqueous solution is proportional to the concentration of the ketone and also to that of the acid.

IV shows the influence of varying acetone concentration in alcoholic solutions containing 5 and 10 grams of water per litre, the experiments being carried out at 0°.

TABLE IV.

Water, 5 grams per litre; $H_2SO_4$ , 0.05 mol. per litre.		Water, 10 grams per litre; $H_2SO_4$ , 0.03 mol. per litre.	
Mols. acetone per litre.	$k \times 10^6$ .	Mols. acetone per litre.	$k \times 10^6$ .
0.816	150.0	1.33	61.0
0.272	51.0	0.272	12.5
3.0	218	5.0	4.9

According to these data, the velocity of the reaction in moist alcoholic solution is proportional to the concentration of the ketone. This result is identical with that previously obtained for a pure aqueous solution, and this identity is clearly contradictory to the hypothesis that the large changes in the reaction velocity which are brought about by the addition of small quantities of water to an alcoholic solution are due to the formation of acetone hydrates which are less active than the free acetone or compounds of acetone with alcohol which might be supposed to be present in alcoholic solution. This is evident from a closer inspection of the two experiments made in alcoholic solution containing 10 grams of water per litre. In these the molar ratios of acetone to water are respectively 1/10 and 1/5. If less active hydrated molecules were formed in the alcoholic solution, such a variation in the relative quantities of acetone and water should undoubtedly give rise to a velocity much greater than the ratio of the acetone concentrations. Since the velocity and acetone concentration ratios are equal, it follows that the observed variations in the rate of tautomeric change are not due to changes in the nature of the solvent medium or to changes in the specific reactivity of the ketone.

The results of measurements of the rate of disappearance of acetone in moist acetone have also led Lapworth to discard the hydrate

formation as a possible explanation of the retardation effect. Moreover, determinations of the refractivity and the dielectric constants of acetone-water mixtures (Drude, *Zeitsch. phys. Chem.*, 1897, **23**, 313; Miss Homfray, *Trans.*, 1905, **87**, 1) indicate that acetone in aqueous solution does not form hydrates more than a very small extent.

On the other hand, strong evidence in favour of the view that the variations in the speed of the tautomeric change are due to differences in the activity of the acid catalyst, is afforded by the fact that so many different reactions, in which an acid plays the rôle of a catalyst, are similarly retarded when small quantities of water are added to the non-aqueous medium in which the reacting substances are dissolved. The view that the anti-catalytic effect of water in these different reactions is not due to any other cause than a change in the availability of the acid is due to Lapworth, and in conjunction with his co-workers, has shown that the changes in availability are the same whether measured by changes in esterification velocity or by the amounts of salt which the acid yields in different moist solutions with a weak monacid base. Mathematical treatment of the conception that the influence of water on acid catalysis is due to a diminution of the quantity of available acid, Lapworth has shown further that this view is in agreement with the generalisations of the ionic theory, and it can be applied to the facts as readily as the original idea of Arrhenius.

Lapworth's views are obviously opposed to the widely accepted theory that the relative catalytic activities of acids in aqueous solution are determined by the concentration of the "hydrogen ions," that is to say, the ions which are mainly responsible for the passage of positive electricity through aqueous solutions of acids. The parallelism between the numbers which represent the relative catalytic activities of the acids on the one hand, and the ionic coefficients as determined by conductivity measurements on the other, is the main factor which has led to the general adoption of the view that the "hydrogen" ions are the active ions in these cases. The gradual accumulation of observations, which support so far the theory that the ions of aqueous solutions are generally hydrated, does not appear to have had any considerable effect on the prevalence of the notion that the electrolytic ion is the catalytic agent.

In particular, this view appears to be adopted by Goldschmidt in a recent summary (*Zeitsch. Elektrochem.*, 1909, **15**, 4) of the results obtained in a series of investigations, in which the esterification of various acids in ethylalcoholic solution under the influence

ent acid catalysts was examined. The parallelism between the ionization constants and the electrical conductivities for various acids used as catalysts and that between the velocity constants for the same acid catalyst at different concentrations and the corresponding ionic concentrations (as measured by the electrical conductivity) are cited as evidence in support of the theory that "proton" ions are the active catalytic agents.

Experiments which were made to ascertain the influence of the concentration of the sulphuric acid as catalyst in the tautomeric formation of acetone seem to show clearly that this theory is untenable. In these experiments, the concentration of the acetone was 272 mol. per litre, and parallel measurements were made with acids containing respectively 0·15 and 0·03 mol. of sulphuric acid per litre. The experimental data are collected in table V, and, indicated in the first column, the temperature of comparison was either 20° or 0°, according to the proportion of water in the aqueous alcoholic solvent. The relative speeds of the reaction for the ionization in the concentration of the acid in the ratio 5:1 are given in the fifth column of the table.

TABLE V.

Nature. Grams of water per litre of solvent.	$k \cdot 10^6$ for $H_2SO_4$	$k \cdot 10^6$		Velocity ratio.	Ratio of electrical conductivities.
		for 0·15 molar $H_2SO_4$	for 0·03 molar $H_2SO_4$		
0°	1000·0	70	14·0	5·0	4·25
0°	400·0	73	11·9	5·2	4·8
0°	50·0	183	31·0	5·9	3·85
0°	10·0	196	12·5	8·5	3·15
0°	5·0	225	26·0	8·6	—
0°	4·5	288	36·0	8·0	—
0°	0·0	920	130·0	7·2	3·55

From the velocity ratios, it is evident that the speed of the ionization is proportional to the concentration of the acid in aqueous solution, and very nearly so in an alcohol-water mixture containing 50 grams of water per litre, but that this is by no means the case in anhydrous alcohol solutions which contain little or no water. In anhydrous alcohol, the speed of the reaction becomes more than seven times as great when the concentration of the acid is increased in the ratio of one from 0·03 mol. to 0·15 mol. per litre. The inequality of the velocity and concentration ratios is even more pronounced in the case of moist alcoholic solutions, and the series of numbers in the table would seem to show that the divergence is greatest when the aqueous solvent contains a certain small proportion of water. Thus, with hydrochloric acid as catalyst, a similar lack of proportionality between the speed of the reaction and the concentration

of the catalyst has been already observed for a large number of esterification reactions in moist alcoholic solution (Kailan, *loc. cit.*). In absolute alcohol, on the other hand, it has been found that in many cases the velocity of esterification is proportional to concentration of the catalyst. This is not, however, always the case, for Kailan has observed that in absolute alcohol the velocity of esterification of the aminobenzoic acids and of 3:5-dinitrobenzoic acid increases more rapidly than the concentration of the catalyst, whilst in the case of 3:4- and 3:5-dihydroxybenzoic acid the velocity increases less rapidly than the concentration of the hydrochloride. In the absence of water, the connexion between activity of the catalyst and its concentration would thus appear to depend on the nature of the catalysed reaction, although in presence of small quantities of water all the available experimental results indicate that the activity of the catalyst increases more rapidly with its concentration.

The difficulty of reconciling these facts with the theory of "hydrogen" ion catalysis has been already pointed out by K and Wegscheider (*loc. cit.*). For sulphuric acid as catalyst the discrepancy between the catalytic activity and the "hydrogen" concentration is shown by a comparison of the velocity ratios given in table V with corresponding ratios for the "hydrogen" ion concentration.

To obtain the necessary data, measurements were made of electrical conductivities of the 0·15 and 0·03 molar solutions of sulphuric acid in various alcohol-water mixtures, and the conductivity ratios thus obtained are recorded in the sixth column of the table.

From the usual ionic point of view, it may be doubted whether the conductivity ratio can be regarded as an exact measure of the "hydrogen" ion ratio, for the conductivity relationships of sulphuric acid in moist alcoholic solutions appear to be of a complex character. On addition of small quantities of water to an alcoholic solution the conductivity falls very considerably until a minimum is reached; beyond this, further increase in the proportion of water causes the conductivity to rise until in pure water it is about twenty times as large as in anhydrous alcohol. Similar observations have been made by Goldschmidt (*Zeitsch. Elektrochem.*, 1909, **15**, 4) in the case of alcoholic solutions of hydrogen chloride, and this behaviour suggests that caution is required in applying the conductivity measurements to the determination of the "hydrogen" ion concentration. In consideration of the small interval of concentration which is involved, it is probable, however, that no serious error will

mitted if the conductivity ratio is taken directly as a measure of relative "hydrogen" ion concentrations.

Comparing the conductivity ratios with the velocity ratios, it is seen that the values diverge much more in the case of alcoholic ions which contain little or no water than they do for a pure aqueous solution. Various hypotheses have been advanced to account for such divergences between the catalytic activities and "hydrogen" ion concentrations in the case of aqueous solutions of acids. An explanation of the very much greater divergences in the case of alcoholic solutions on similar lines seems scarcely possible. On the contrary, the deviations are such that the conclusion seems reasonable that the active catalysts in alcoholic solution are not the ions which are responsible for the electrical conducting power.

In favour of this conclusion is the fact that the catalysing power of sulphuric acid in dilute alcoholic solution is about a hundred times as great as it is in a corresponding aqueous solution, whereas the "hydrogen" ion concentrations appear to be nearly equal. In the case of a 0·05 molar acid, the degree of ionisation in aqueous solution is approximately 0·6, and, according to Kremann and Sert (*Monatsh.*, 1910, **31**, 195), the degree of ionisation for an alcoholic solution (containing 0·6 per cent. of water) is about 0·5. These data indicate that the concentration of the "hydrogen" ions in aqueous and alcoholic solutions of this order of concentration is approximately the same, whereas the velocity data indicate that a catalytically active component is present in alcoholic solution in much greater concentration than in a corresponding aqueous solution.

The observed facts are thus seen to be irreconcilable with the hypothesis that acid catalysis is due to "hydrogen" ions, but, on the other hand, they appear to harmonise with the theory of acid dissociation advanced by Lapworth. According to this, the catalytic activity of an acid is determined by its availability, and if we postulate the existence of free hydrogen ions in solutions of acids, their concentration furnishes a measure of the availability. At a given concentration of acid, the proportion of free hydrogen ions is much greater in the case of an alcoholic solution than in that of an aqueous solution, although the concentrations of the positive ions—the ethylhydroxonium ions in the one case, and the oxonium ions in the other—may be, and probably are, of the same order of magnitude.

The chief results obtained in this investigation may be summarised as follows:

Data are recorded showing the influence of the medium on the

rate of tautomeric change of acetone in presence of sulphuric acid as a catalyst for alcohol-water mixtures, ranging from pure to anhydrous alcohol.

2. In anhydrous alcohol the speed of the reaction is more than a hundred times as great as in water. On addition of quantities of water to the alcoholic solution, the velocity is greatly diminished.

3. In alcoholic solutions the speed of the reaction is proportional to the concentration of the ketone, but increases much more rapidly than the concentration of the catalyst or the concentration of "hydrogen" ions.

4. It is shown that the observations are inconsistent with the theory of "hydrogen" ion catalysis, but that they appear capable of interpretation on the lines of Lapworth's theory of association.

For assistance in preliminary experiments, I desire to express thanks to Mr. R. Wheatley, B.Sc.

PHYSICAL CHEMISTRY LABORATORY,  
THE UNIVERSITY,  
LEEDS.

## II.—*Cryoscopic, Ebullioscopic, and Association Constants of Trimethylcarbinol.*

By WILLIAM RINGROSE GELSTON ATKINS.

It was suggested by Professor E. A. Werner that trimethylcarbinol might be a useful solvent for molecular-weight determination by cryoscopy, as it was the only one of the lower alcohols that had a convenient melting point, and was not likely to dissociate compared with other organic compounds which were being studied by him.

As the divergence between the values of  $E$ , the molecular law of freezing point, as found by experiment and as calculated from the heat of fusion, was very remarkable, the study of the ebullioscopic and association constants was also undertaken.

Trimethylcarbinol was found by Paternò and Ampola (*Gazz.* 1897, **27**, i, 481) to give one minimum on the freezing point diagram with *p*-bromotoluene, and one with thymol; they point out that the freezing points of these mixtures cannot be even approximately calculated by the formula  $E = \frac{RT_0}{100s}$ . With phenol they find a complex curve, showing two maxima and three minima. Calculated

[heir data shows that the compounds  $(\text{CH}_3)_3\text{C}\cdot\text{OH}, 2(\text{CH}_3)_2\text{C}\cdot\text{OH}, \text{C}_6\text{H}_5\cdot\text{OH}$  are present, making allowance for the nature of the curves.

ernò (*Atti R. Accad. Lincei*, 1907, [v], **16**, ii, 153) has shown he compound  $(\text{CH}_3)_3\text{C}\cdot\text{OH}, 2\text{H}_2\text{O}$  exists from a study of the ng point diagram, but viscosity determinations show that it pletely dissociated a few degrees above the melting point of ure alcohol. Subsequently, Paternò and Mieli (*Atti R. Accad.*, 1908, [v], **17**, i, 396) drew the conclusion that there o correlation between the density curve and the temperature- sition curve for the phenol-trimethylcarbinol mixture.

melting point of the alcohol,  $25.53^\circ$ , is abnormally high for eries. It seems that this is due to a combination of two s. It has been pointed out by Carnelley (Smiles, *Chemical titation and Some Physical Properties*, p. 200) that among rides the compound with the more symmetrical structure es the higher melting point, whilst Markownikoff has shown the compound with the more highly branched chain of carbon i melts at the higher temperature. Now trimethylcarbinol is ice the most symmetrical alcohol, for the methyl group =15) is very close to the hydroxyl group (OH=17) in weight, he most highly branched form of carbon atom chain is also at, hence the remarkably high melting point.

#### *Cryoscopic Constant.*

hlbaum's trimethylcarbinol was purified by distillation with ne (S. Young, *Fractional Distillation*, p. 233), and placed in inner tube of a Beckmann apparatus, with stirrer and drying attached. The following substances were employed as solutes determine the constant: *p*-dibromobenzene, acetanilide, thioamide, *p*-toluidine, and  $\alpha$ -naphthylamine. The details are given e experimental part of the paper. The values of  $E$  ranged 134.5 to 82.5 for *p*-dibromobenzene as the concentration used, from 154.4 to 72.9 for acetanilide, from 152.5 to 137.4 naphthylamine, whilst thiocarbamide gave  $E=83.7$ . Taking prand's (*Compt. rend.*, 1903, **136**, 1034) value for the latent of fusion,  $s=20.978$  cal., and evaluating the expression  $E=\frac{RT_c}{100s}$   $R=1.991$  cal. and  $T_c$  is the melting point on the absolute it is found that  $E$  (calc.) = 84.5.

appears at first sight as if the determinations had been made substances which dissociated in solution, and thus gave in e solutions a depression nearly twice as great as would be

expected, whilst in concentrated solutions the theoretical value more nearly approached. However, the chemical evidence strongly against the dissociation of the solutes employed to any like the extent required, at any rate. Moreover, it was found that the pure alcohol was practically a non-conductor, and when a *p*-toluidine was dissolved in it, no difference could be detected conductivity, although a sensitive galvanometer was used.

To test the possibility of the unexpectedly great lowering of freezing point being due to the hygroscopic nature of the liquid, the apparatus was allowed to remain for one day, when depression was found to be only 0.02° lower than on the previous day. Taking into account the difficulty of obtaining two consecutive readings with this solvent, which differ by less than 0.01°, it is clear that the slow absorption of water will not explain the results. The decrease in  $E$  with increase in concentration is against such an explanation. Separation of the solute with the solvent would, of course, lower the value of  $E$ , and so need not be considered further.

There still remains the possibility of error having arisen through the too great separation of the solvent on freezing, and through radiation effect from the cooling bath. Accordingly, fresh determinations were made, using *p*-dibromobenzene as solute, the temperature of the bath being -0.8° and -2.5° below that of the solution. The value thus obtained for  $\Delta$  was corrected by Ray's equation (*Compt. rend.*, 1897, **125**, 751),  $\Delta = \Delta_{\text{obs.}}(1 - KS)$ , where  $S$  is the supercooling in degrees, and  $K$  is a constant obtained from the expression:

$$K = \frac{1}{L} \left( 1 + \frac{r}{R} \right) \pm \left( 1 + \frac{r}{R} \right) \frac{t}{T} \times \frac{1}{SL},$$

in which  $L$  is the heat of fusion of the solvent,  $r$  the water equivalent of the part of the apparatus wetted,  $R$  the water equivalent of the solvent used,  $t$  the time from freezing to steady temperature,  $T$  the time for the apparatus to cool or warm 1° by radiation. The resultant value was  $E = 128$ , which agrees well with the determinations of  $E$  in the main series.

Thus for a dilute solution of *p*-dibromobenzene the value of 128, whereas theory requires it to be 84.5. The discrepancy may be accepted as a fact, and an explanation attempted. On this basis the nearly normal values obtained with more concentrated solutions are to be accounted for as due to association of the solutes, which is just what is to be expected, especially with substances containing amino-groups. *p*-Dibromobenzene was selected as a solute as it is in every way a "normal" substance, giving a unimolecular line on fusion (*Crompton, Trans.*, 1897, **71**, 925). Accordingly,

for  $E$  found with it has been taken in preference to a mean

of interest to calculate the values of  $E$  from data given by id (*loc. cit.*) for the alcohol-water concentration-temperature m. Here  $E=88.8$  for an addition of 1.34 per cent. of water, falls off considerably, due no doubt to association of the water. 5.74 per cent. of water,  $E=64.6$ , and at the minimum point curve,  $E=45.1$ . As the depression of freezing point amounts for 1.34 per cent., it is probable that a higher value for  $E$  be arrived at for smaller depressions. Considering the other his curve, in which water is the solvent, with 5.79 per cent. alcohol, we obtain  $E=19.1$ , and with 11.19 per cent.,  $E=25.1$ . molecular weight of the alcohol, of course, varies in the inverse on. Taking  $E=18.7$  for water, then  $M=72$  and 55 at the five concentrations. Even allowing for the calculations being on a percentage basis, not as grams per 100 grams, the results appear to indicate dissociation of the alcohol, an appearance comparable with the behaviour of certain substances in the 1 as solvent.

however, with Crompton (*loc. cit.*), we admit that the portion of the solvent has to be taken into account as well as the solute, we have to consider his third case, that of a molecular solute in an associated solvent, and must calculate  $\frac{RT^2}{M} \times \frac{x}{a}$ , and  $E = \frac{RT^2}{100s} \times \frac{x}{a}$ , where "a" is the association factor vapour, "x" the association factor of the liquid, and  $s$  and  $R$  the heat of fusion and gas constant in calories. Then, as  $s=1.9$  from 26°–36°, as found by Ramsay and Shields' d (Carrara and Ferrari, *Gazzetta*, 1906, **36**, i, 419):

$$E = \frac{1.9917T^2}{100s} \times \frac{1.9}{1.0} = 160.5.$$

This value for  $E$  is sufficiently high to include all the values by experiment, the lower values being, as before, attributed to dissociation of the solute. As, however, the above relation of id has been rejected (Nernst, *Theoretical Chemistry*, Eng. 4th ed., p. 268), this explanation can hardly be regarded satisfactory.

Turning now to van't Hoff's equation,  $E = \frac{RT^2}{100s}$ , it is seen that  $s$  is the only value open to question. Taking the experimentally found  $E=128$ , and using it to calculate  $s$ , we obtain  $s=13.84$  cal., instead of 20.98 cal. (de Forerand, *loc. cit.*). De Forerand had as to whether the definite state of the solid was reached at If it is not, different values would, of course, be found

according to the length of time the alcohol remained solid determined  $C_s$  between  $-21.5^\circ$  and  $+14^\circ$ , and concludes : only increases between his first determination and his last by cent. at the most. Hence  $s$  cannot change either. In his experiment, however, the alcohol was kept at  $-21.5^\circ$  for four days. Thus a quick change would escape detection by his method, the low temperature producing even greater rapidity. He proceeded further to test his values by the relation he had previously derived:

$$\frac{L+S}{T} = 30 \text{ (28 to 32)} (\text{Compt. rend.}, 1903, \textbf{136}, 945), \text{ where } T$$

absolute boiling point, and  $L$  and  $S$  are the molecular heats of vaporisation at the boiling point and of fusion respectively.

$$\frac{L+S}{T} = \frac{9428 + 1948}{355.8} = 30.85, \text{ the agreement being satisfactory.}$$

similar calculation can be made, using  $s=13.84$  and conse-

$$S=1024, \text{ we obtain } \frac{9426 + 1024}{355.8} = 29.66, \text{ which is still within}$$

limits of the constant.

The abnormally low value of Crompton's relation (*loc. cit.*)  $\frac{10sd}{T} = 1.00$  (where  $d$  is the density at the melting point,  $w$  represented by  $T$  on the absolute scale), which trimethylol propane affords, namely, 0.54, may point to  $20.98^\circ$  being too low a value for  $s$ , but it seems far more likely that it is due to the relatively high value of  $T$ , due to the influences referred to before.

Now it is quite possible that in the case of trimethylol propane we are dealing with a substance possessing two crystalline modifications, the unstable rapidly passing into the stable. The number of facts seems to point to this conclusion. To begin with, when the alcohol is supercooled and suddenly solidifies, a mass of needle crystals is produced. After keeping for a day or two, none of this form can be found, but a number of plate forms have appeared, which are often hexagonal in shape. This stage is reached in two or three hours but few of the needle form are to be found. Both forms illuminate and are extinguished when rotated in plane-polarised light. The minute ones and the longer ones formed more slowly give greys of the order of 10% to 20% of the maximum intensity, whilst the larger ones give strong colours. De Forcrand (*loc. cit.*) describes the crystals as if from a flattened orthorhombic prism with modifications, but does not mention the needle form. Professor J. J. Johansen kindly examined both forms for me, and, while agreeing that the large crystals were orthorhombic, did not think it possible to say to what system the needles belonged. In the crystallisa-

ly occurring minerals, monoclinic substances very frequently an acicular form, and most organic compounds belong to this, but, on the other hand, the birefringence of both plates needles was very much the same. To sum up, examination of crystals in polarised light gives no certain evidence for or against existence of two modifications.

attempt was made to study the change by taking a series of photographs under polarised light, as described by Pope (*Trans.*, 35, 455) in his work on chloral hydrate. However, owing to difficulty of preventing the crystals from melting without a film of dew on the slide, I have not as yet been able to obtain photographs.

may be thought that in the passage from one crystalline con- to another the change in the heats of fusion would not be at great as from 13.84 cal. to 20.98 cal., for in the case of ice and monoclinic sulphur the difference is small. With chloral hydrate, however, Berthelot (*Compt. rend.*, 1880, **90**, 812, found  $s=17.52$  cal. for the freshly melted crystals, and 13 for those which had remained solid for some time. Pope has recently proved that chloral hydrate was polymorphic, and a number of substances show these phenomena in a lesser

that the discrepancy in the two heats of fusion of trimethylol is due to the existence of two crystalline modifications, very unstable, seemed to me to be all the more probable, as Ann (*Ann. Phys. Chem.*, 1899, [iii], **68**, 553, 629) has found a point for the liquid and two solid phases at  $60^{\circ}$  and 1700 atmos pressure. From the triple point two melting-point curves pass, and also a transition curve, giving the temperatures and pressures at which the modifications change in the solid state. From the theory of crystals which are absolutely stable only under high pressures, Skrabal (*Zeitsch. physikal. Chem.*, 1910, **73**, 171) points out that there is a connexion between the velocity of a change and the stability of the reaction products in such a way that the more violent the reaction the greater is the possibility of obtaining the less stable products. This, he states, is in accord with the results of experiment. Now, the separation of the needle crystals of trimethylcarbinol is very rapid, and it seems probable that this is the form which Tammann found to be stable only at high pressures and temperatures. Its great instability at the ordinary temperature and atmospheric pressure accounts for its rapid disappearance, so shows why the heat of fusion of the two forms is so great.

*Ebullioscopic Constant.*

Taking the mean of values obtained with *p*-dibromocarbamide, and naphthalene, the constant is found to have value  $E=17\cdot45$ . Lower values,  $E=13\cdot77$  and  $E=13\cdot1$  obtained with thiocarbamide and stearic acid respectively, calculation from van't Hoff's equation gives  $E=19\cdot78$ .

D. E. Tsakalotos (*Compt. rend.*, 1907, **144**, 1104) gives relation:

$$E = M \times \frac{1}{475 \log \frac{T}{T'} - 0.35},$$

where  $T$  is the absolute boiling point. This gives  $E=19$  in agreement with van't Hoff's equation being good. As, however, associated liquid is being considered, the expression  $\frac{E}{E_x}$  should be used, where  $E$  is the value for another member of homologous series considered. Taking  $E=11\cdot5$  for ethyl ether the value of  $E_x$  is 18.97. This is in closer agreement with experimentally determined value.

Baume and Tsakalotos (*Compt. rend.*, 1907, **144**, 373) give equation  $L = \frac{RT^2}{JM_p} \frac{dp}{dT}$ , where  $J$  is the mechanical equivalent of  $M_p$ , taking  $R = 0.024$  and  $R$  is the gas constant. Combining this with  $L = \frac{0.024}{E} \frac{dp}{dT}$ , taking  $J = 0.01M_p$ , we get  $\frac{dp}{dT} = \frac{R}{E}$ .

Not being able to find a recorded value for  $\frac{dp}{dT}$  for trimethyl ether, that for propyl alcohol was taken,  $\frac{dp}{dT} = 28.8$ . The above gives  $E = 19.53$ , in very close proximity to the previous values.

If, on the other hand, the value of  $E$  from van't Hoff's equation is taken, calculation gives  $\frac{dp}{dT} = 28.4$  for the tertiary alcohol.

To sum up we have:

Experimental.	van't Hoff (calc.).	Tsakalotos (calc.).	Baume and Tsakalotos
	$E = 17.45$	$19.78$	$19.17$ and $18.97$

It thus appears that the experimental value is too low for reason. Further determinations are desirable.

De Forcrand's value for  $L$  was employed. In his  $L = \frac{9436}{T} = \frac{9436}{355.8}$  is given as 22.49, evidently a misprint for 26.5, close to the value given by the other alcohols.

*Association Factor.*

Calculation was made from Ramsay and Shields' formula from  $f\gamma_t$  recorded in the experimental portion of the paper. The  $f$  Carrara and Ferrari (*loc. cit.*), with which I subsequently acquainted, are given for comparison;  $x$  denotes the  $f$  factor,  $t$  represents the range of temperature.

$t.$	$x.$	$t.$	$x$ (Carrara).
-5-46-4°	1.406	26-36°	1.924
7-46-6	1.370	36-40	1.515
4-80-0	1.295	40-45	1.268
-6-79-5	1.313	Mean 36-45	1.391
-0-47-0	1.388		

Agreement between the two sets of values is satisfactory. The use of  $x$  at the lower temperatures is to be noted. It is of interest to compare these values with those arrived at by Walden's method (*Zeits. physikal. Chem.*, 1908, **65**, 129). He gives  $\frac{\lambda_e}{a_e^2} = \text{const.}$  where  $\lambda_e$  denotes the latent heat of evaporation at the boiling point and  $a_e^2$  is the specific cohesion at the same temperature. Here

the calculation shows some abnormality, for trimethylcarbinol  $\frac{\lambda_e}{a_e^2} = 24.8$ . Again, he gives  $\frac{M a_e^2}{T_e} = 1.16$ , and the divergence of the constant from its normal value may be taken as a measure of the abnormality. The calculated constant is 1.06, which gives  $x = 1.094$  at the boiling point.

Land Mojoiu (*J. Chim. phys.*, 1909, **7**, 169) have shown that the cohesion is approximately constant, varying from 0.0173 to 0.0188, whereas the association factor varies from 0.0163 to 0.0205. They apparently take  $a^2 = \frac{2\gamma}{\rho}$ .

Comparing thus, the tertiary alcohol gives  $\frac{\lambda_e}{a_e^2} = 0.0253$ , a considerable discrepancy.

Păinescu has studied association by a different method (*J. Chim.*, 1908, **6**, 552). He finds for unassociated liquids that the following relation holds:  $\left(\frac{T}{100D_0}\right)^2 = n$ , where  $n$  is the number of atoms in the molecule. By a comparison of  $n$  (calc.) with  $n$  (theory), the degree of association may be estimated. Taking Paternò's value for  $D_0$  of trimethylcarbinol gives  $n = 19.1$  (calc.),  $n = 15$  (theory); hence  $\alpha = 1.27$ , which does not agree with the results of the other workers. As it might not be permissible to use this value for  $D_0$ , we must

since the melting point is  $25\cdot43^\circ$ , the constant was calculated for pentane and hexane, as being in every way normal liquids, at  $30^\circ$ , taking the densities given by Young (*Sci. Proc. Roy. Dublin Soc.*, 1910, **12**, No. 31). Then for  $\frac{T}{D\sqrt{n}} = \frac{T'}{D'\sqrt{n'}}$  = 100 (approx.) the values 121·5 and 117·5 were obtained for pentane and hexane respectively at  $30^\circ$ , also 116·2 and 113·0 at  $0^\circ$ . Substituting the mean constant at  $30^\circ$ , and correcting for the constant at  $0^\circ$  being 114·6 instead of 100, the value  $x=1\cdot12$  at  $30^\circ$  is obtained. The agreement is no better than before. To sum up, the values arrived at by Ramsay and Shields' method agree fairly with that found by Walden's equation for the boiling-point temperature. It will be noticed that the former measurements give the mean value over a range of temperature, whilst the latter give the value at a definite temperature. The results obtained by Longuinescu's relation do not agree with those of the two previous methods, and judging by the wide divergence of the constant even with normal liquids, such as pentane and hexane, but little more than qualitative results can be obtained from this method.

#### EXPERIMENTAL.

##### *Cryoscopic Constant.*

The apparatus used was the ordinary Beckmann, with air space between the freezing tube and the outer jacket, which was also an air space, as the freezing point of the alcohol was only slightly above room temperature. When the solvent was supercooled  $0\cdot3^\circ$  to  $0\cdot6^\circ$ , the appearance of needle crystals was extremely rapid, and the temperature rose. A steady state was soon reached, but as a considerable quantity of the solvent had crystallised out, the tube was withdrawn, and the heat of the hand sufficed to melt most of the crystals. The tube was then replaced and allowed to steady down. It reached a point  $0\cdot04^\circ$  to  $0\cdot05^\circ$  above the former reading. This was taken as the true freezing point. It is worthy of note that this is close to the correction calculated from Raoult's formula and applied in the last experiment.

The alcohol used all distilled over between  $82\cdot35^\circ$  and  $82\cdot55^\circ$  under 760 mm. pressure (corr.). In the tables below,  $s$  denotes the weight of solute dissolved in 100 grams of solvent;  $\Delta$  the depression of freezing point;  $E$  the molecular lowering constant as calculated from  $\Delta$ ; and  $M$  the molecular weight of the solute as calculated from  $\Delta$  and the value of  $E$  obtained from van't Hoff's formula (namely, 81·5);  $t$  denotes the temperature of the outer air jacket, the inner air jacket being about  $0\cdot7^\circ$  higher. From 10 to 12 grams of alcohol were used in each experiment.

Solute: *p*-dibromobenzene,  $M = 236$ .

<i>s.</i>	$\Delta.$	<i>E.</i>	<i>M.</i>	<i>t.</i>
2.27	1.18	122.8	163	19.6°
5.42	2.31	109.5	198	21.1
8.99	3.14	82.5	242	—
10.83	(3.61)	—	—	19.9

Fine crystals of the solute separated before the solvent froze.

0.81	0.17	128.0	155	19.7°
1.04	0.47	106.6	187	—

Solute: acetanilide,  $M = 135$ .

Solvent contained about 1 per cent. of *p*-dibromobenzene.

<i>s.</i>	$\Delta.$	<i>E.</i>	<i>M.</i>	<i>t.</i>
0.38	0.43	154.4	75	19.1°
1.15	0.97	112.3	100	—
1.93	1.47	102.6	111	—
6.31	8.41	72.9	156	—

Solute: thiocarbonamide,  $M = 76$ .

<i>s.</i>	$\Delta.$	<i>E.</i>	<i>M.</i>	<i>t.</i>
0.33	0.465	83.7	61	19.9°

Solute: *p*-toluidine,  $M = 107$ .

<i>s.</i>	$\Delta.$	<i>E.</i>	<i>M.</i>	<i>t.</i>
0.27	0.37	147.7	61.7	21.9°
0.46	0.65	152.5	59.3	—
0.78	1.07	147.2	61.4	—
1.93	2.50	138.6	65.3	—
3.26	4.19	137.4	65.8	—

Solute:  $\alpha$ -naphthylamine,  $M = 143$ .

<i>s.</i>	$\Delta.$	<i>E.</i>	<i>M.</i>	<i>t.</i>
0.31	0.247	112.1	108.6	21.7°
0.66	0.51	116.9	103.4	—
1.16	0.89	109.8	110.0	—
2.10	1.41	95.8	126.1	—
4.05	2.43	85.7	141.0	—
6.71	3.73	79.4	152.2	—

Solute: water,  $M = 18$ . From Paternò's curve data.

$H_2O$ per cent.	$\Delta.$	<i>E.</i>	<i>M.</i>
1.34	6.6	88.8	17.1
2.53	12.2	86.8	17.5
3.64	15.3	75.5	20.0
4.55	18.0	67.3	21.3
5.74	20.6	64.6	23.3
8.00	25.4	57.0	23.7
12.03	30.2 (max. $\Delta$ )	45.1	33.6

Solute: trimethylcarbinol,  $M=74$ . Water as solvent.

From Paternò's curve data.

Alcohol per cent.	$\Delta$ .	$E$ .	$M$ .
5·79	1·5	19·2	72
7·74	2·4	23·0	61
11·19	3·8	25·1	55

### Revision Series.

Solute: *p*-dibromobenzene,  $M=236$ .

$s$ .	$\Delta$ .	$E$ .	$M$ .	$t$ .
0·295	0·167	133·6	149·4	0·8° below m. p. of alcohol
1·91	{ 1·12 (obs.) 1·04 (corr.)	{ 145·0 128·1	155·6	} 2·8° below m. p. of alcohol

The correction was made from Raoult's equation,

$$\Delta = \Delta_{(\text{obs.})} (1 - KN),$$

where

$$K = \frac{L}{R} \left( 1 + \frac{r}{R} \right) \pm \left( 1 + \frac{r}{R} \right) \frac{t}{T} \times \frac{1}{SL'}$$

(The notation has been previously explained.)

The second term is negligible, as  $t=1$  min.,  $T=20$  min., and  $S=0·08^\circ$ . However, as  $r=14·1$ , and  $R=14·58 \times 0·722$ , the correction as a whole is considerable.

Constants of trimethylcarbinol employed in calculations throughout the paper:

Melting point  $25·53^\circ$ , and boiling point  $82·55^\circ$  (S. Young, *Fractional Distillation*).

Melting point  $25·43^\circ$ , and boiling point  $82·8^\circ$ , at 761 mm. pressure.  
(De Forcrand.)

Sp. heat, liquid,  $C_l=0·722$  from  $25·45^\circ$  to  $44·80^\circ$ . (De Forcrand.)

Sp. heat, solid,  $C_s=0·580$  from  $-21·5^\circ$  to  $+14^\circ$ . (De Forcrand.)

Heat of fusion,  $s=20\ 978$  cal. } At  $25·45^\circ$ . (De Forcrand.)

Molecular heat of fusion,  $S=1552$  cal. } At  $25·45^\circ$ . (De Forcrand.)

Heat of vaporisation,  $l=127·38$  cal. } At  $82·8^\circ$ . (De Forcrand.)

Molecular heat of vaporisation,  $L=9426$  cal. } At  $82·8^\circ$ . (De Forcrand, *loc. cit.*)

$\rho'_v=0·81388 - 0·001256t$  (Paternò, *Atti R. Accad. Lincei*, 1907, [v], 16, ii, 153). Paternò actually gives  $0·0001256t$ , but I believe this to be a misprint, as it does not agree with his own values for  $\rho'_v$  or with the values of Thorpe and Jones (Trans., 1893, 63, 278).

### EBULLIOSCOPIc Constant.

The apparatus used had a platinum wire fused in the bottom and was surrounded by a vapour jacket. This was filled with pure

benzene, the boiling point of which differs only by 2·5° from that of the alcohol. There was not enough of the pure alcohol to use as a jacket. A series of readings was taken in each case, and chips of a clay pipe stem were added from time to time to avoid superheating. The stem had been boiled with water after being broken up, and was heated to redness and allowed to cool, just before use.

Solute: *p*-dibromobenzene,  $M=236$ .

<i>s.</i>	$\Delta.$	<i>E.</i>
2·01	0·122	14·31
5·81	0·371	15·05
8·27	0·578	16·50
11·67	0·850	17·21

Solute: thiocarbamide,  $M=76$ .

<i>s.</i>	$\Delta.$	<i>E.</i>
0·81	0·140	15·14
1·18	0·213	13·77

Solute: carbamide,  $M=60$ , in presence of the thiocarbamide of the previous series.

<i>s.</i>	$\Delta.$	<i>E.</i>
0·695	0·205	17·69
2·07	0·596	17·24

Solute: stearic acid,  $M=284$ , in presence of carbamide and thiocarbamide, as before.

<i>s.</i>	$\Delta.$	<i>E.</i>
1·13	0·049	12·50
3·05	0·178	13·17

Solute: naphthalene,  $M=128$ , in presence of thiocarbamide, carbamide, and stearic acid, as before.

<i>s.</i>	$\Delta.$	<i>E.</i>
1·87	0·150	17·66

Calculation from  $E = \frac{RT^2}{100f}$  gives the value 19·78 as against 17·45,

a mean of the values obtained for carbamide, naphthalene, and the highest value for *p*-dibromobenzene. It will be noticed that there is a rise in the value of *E* with rise in concentration, which is the very reverse of the effect of association. This is most marked in the *p*-dibromobenzene series, and is quite beyond the range of experimental error in determining the boiling point. The question

needs further investigation, but it seems possible that it may be explained by the adsorption of the solute by the pipeclay chips, which were present in quantity.

#### *Association Factor.*

The value of  $\gamma$  was ascertained by measuring the height of the liquid in a capillary tube at various temperatures, using pure ethyl ether, carbon disulphide, and benzene to give constant temperature vapour jackets. A thermometer capillary was used, after its uniformity of bore had been tested. All measurements were made on a falling column. Before taking a reading, the temperature was maintained constant to  $0^{\circ}\text{05}$  for fifteen to twenty minutes. In the tables,  $h$  denotes the height in scale divisions, one division =  $0^{\circ}0798$  cm. Radius of tube =  $0^{\circ}0096$  cm., as found by calibration with mercury.

#### *Series A.*

The melting point of the alcohol used was  $23^{\circ}95$ ;  $\rho_4^{25} = 0^{\circ}7829$ ; from this,  $\rho_4^0 = 0^{\circ}8143$  was found by Paternò's formula, and the other values were calculated by it from the above value.

$h$ ,	$\rho$ ,	$t$ ,	$\gamma$ , in dynes.
68.1	0.7703	34.5	19.45
65.1	0.7556	46.4	18.23
56.1	0.7133	80.0	17.84
-	0.7103	82.5	17.81 (calc.).

#### *Series B.*

The alcohol employed distilled over between  $82^{\circ}51$  and  $82^{\circ}55$  under 770 mm. pressure (corr.).

$h$ ,	$\rho$ ,	$t$ ,	$\gamma$ ,
67.9	0.7703	34.7	19.38
64.9	0.7553	46.6	18.17
56.0	0.7140	79.5	17.82
-	0.7103	82.5	17.79 (calc.).

From these values, the association factor  $x$  was calculated, employing the expression:

$$Mx = \frac{\{ -2.12(t_0 - t_1) \}^2}{\{ \gamma_0 \rho_0^{25} - \gamma_1 \rho_1^{25} \}},$$

The values of  $\gamma$  at the boiling point  $82^{\circ}5$  were calculated by means of the coefficients 0.012 and 0.011 for the change in the value of  $\gamma$  expressed in dynes per degree in series A and B respectively. These were derived from the  $46$ – $80$ ° range. The surface-tension measurements were performed in the presence of dry air, not in a

vacuum. That this is quite permissible has been shown by Renard and Guye (*J. Chim. phys.*, 1907, **5**, 81).

I take this opportunity of expressing my thanks to Professor S. Young for the use of apparatus and for the benefit of his advice.

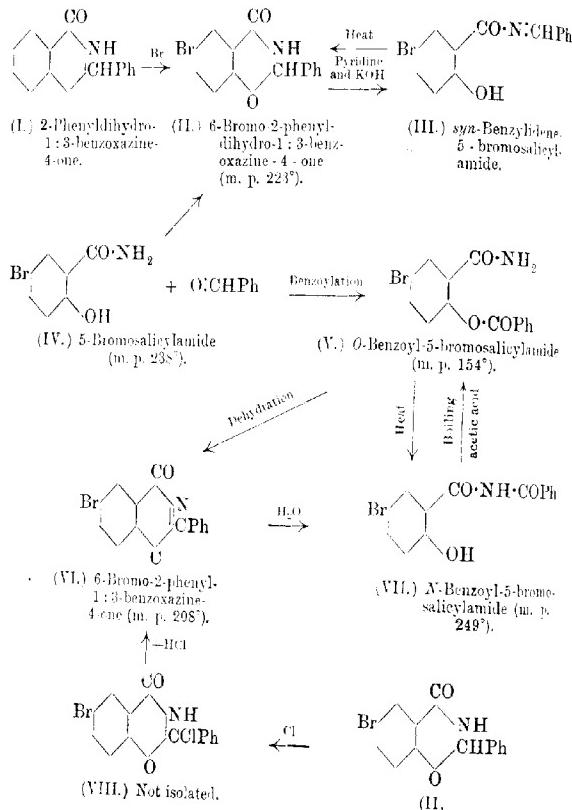
UNIVERSITY CHEMICAL LABORATORY,  
TRINITY COLLEGE, DUBLIN.

**III.—6-Bromo-2-phenyldihydro-1 : 3-benzoxazine-4-one  
and Related Derivatives.**

By ERNEST CHISLETT HUGHES and ARTHUR WALSH TITHERLEY.

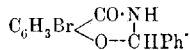
In a previous paper (Trans., 1910, **97**, 1368) the authors described a series of chloro-derivatives in connexion with the study of the action of chlorine on 2-phenyldihydro-1 : 3-benzoxazine-4-one (I). The behaviour of the latter compound with bromine has now been examined, and it has been found that simple bromination occurs in the benzene nucleus, yielding 6-bromo-2-phenyldihydro-1 : 3-benzoxazine-4-one (II), whilst no substitution of the 2-hydrogen atom takes place such as occurs in the corresponding experiments with chlorine; that is, the expected unsaturated derivative, 6-bromo-2-phenyl-1 : 3-benzoxazine-4-one (VI), is not produced. This compound, however, can be obtained by submitting 6-bromo-2-phenyldihydro-1 : 3-benzoxazine-4-one (II) to the action of chlorine instead of to the further action of bromine, when in benzotrichloride solution at 110° substitution occurs at position 2, yielding the intermediate 2-chloro-6-bromo-derivative (VIII), which immediately loses hydrogen chloride as in the case of the 2 : 6-dichloro-compound (*loc. cit.*). It is evident that the hydrogen atom at position 2 is readily affected by chlorine, but not by bromine. Further, the unsaturated ring compound (VI) has been synthetically prepared from *O*-benzoyl-5-bromosalicylamide (V) (obtained by pyridine benzylation of 5-bromosalicylamide, IV) by the same dehydration method as that used in the preparation of the corresponding 6-chloro-compound. Further, the constitution of the dihydro-compound (II) has been confirmed by its independent synthesis from 5-bromo-salicylamide (IV) and benzaldehyde. The properties of the two bromo-oxazone compounds (II and VI) are in every respect similar to those of the corresponding chloro derivatives, and whilst 6-bromo-2-phenyldihydro-1 : 3-benzoxazine-4-one (II) on treatment with

pyridine and alkali yields a labile *syn*-benzylidene-5-bromosalicyl amide (III), and with boiling dilute alkali, benzaldehyde and 5-bromosalicylamide, 6-bromo-2-phenyl-1:3-benzoxazine-4-one (VI) is converted by treatment with alkali (or acid) into *N*-benzoyl-5-bromosalicylamide (VII), which on further hydrolysis gives 5-bromosalicylamide and benzoic acid. The same reversible rearrangement phenomena have been observed between the corresponding 5-chloro-derivatives and *O*- and *N*-benzoylsalicylamides. The above relations are expressed in the scheme:



## EXPERIMENTAL.

*6-Bromo-2-phenyldihydro-1:3-benzoxazine-4-one,*



(1) *Bromination of 2-Phenyldihydro-1:3-benzoxazine-4-one.*—Bromination proceeds easily in the cold, but owing to a secondary reaction, in which some water appears to be produced, a considerable quantity of bromosalicylamide and benzaldehyde is formed as a by-product. A solution of 10 grams of 2-phenyldihydro-1:3-benzoxazine-4-one in chloroform was gradually treated with 5·2 grams of bromine; the red colour rapidly disappeared, and a pale yellow solid separated (4·5 grams), which, after two hours, was collected and recrystallised from alcohol. It melted at 235°, gave a strong violet colour with ferric chloride, dissolved with slight fluorescence in sodium hydroxide, and was identified as 5-bromosalicylamide. (Found, N = 6·45; Br. = 36·68. Calc., N = 6·48; Br = 37·03 per cent.)

From the chloroform filtrate, which contained impure benzaldehyde, 6-bromo-2-phenyldihydro-1:3-benzoxazine-4-one (4·6 grams) was isolated as a pale yellow solid by evaporation and digestion with cold dilute sodium hydroxide. It was obtained pure, by recrystallisation from hot benzene, in fine, colourless needles, melting at 223°:

0·3506, by Kjeldahl's method, required 11·2 c.c. N/10-HCl. N = 4·42. 0·2186 gave 0·1340 AgBr. Br = 26·08.

$\text{C}_{14}\text{H}_{10}\text{O}_2\text{NBr}$  requires N = 4·61; Br = 26·31 per cent.

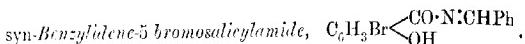
The compound is sparingly soluble in cold alcohol, benzene, or acetone, moderately so in cold chloroform, and readily soluble in hot alcohol or benzene, from both of which it crystallises well on cooling. It is readily decomposed on warming with dilute sodium hydroxide, giving benzaldehyde.

(2) *Condensation of 5-Bromosalicylamide and Benzaldehyde.*—The requisite 5-bromosalicylamide (described by Kauschke, *J. pr. Chem.*, 1895, [ii], 51, 211) was obtained by adding 60 grams of bromine gradually to a boiling solution of 50 grams of salicylamide in 1500 c.c. of chloroform. A vigorous reaction took place, the colour of the bromine disappearing immediately, and a copious precipitate of the bromo-derivative being formed. The chloroform was finally distilled off in order to remove the hydrogen bromide, which proved troublesome unless eliminated at this stage, and the solid collected and washed with a little ether. After recrystallisation from alcohol, it melted at 238° (Kauschke gives 232°). The condensation of 5-bromosalicylamide and benzaldehyde was easily

effected. Five grams of bromosalicylamide were dissolved by warming in 20 c.c. of benzaldehyde, and 0·5 c.c. of alcoholic hydrogen chloride added. After heating at 100° for a few minutes and allowing to cool slowly, 6-bromo-2-phenyldihydro-1:3-benzoxazine-4-one separated, practically pure, as a thick mass of colourless crystals (6 grams), which were collected and washed with a little alcohol and ether. It melted at 219°, and, after recrystallisation from alcohol, at 223°. The substance was identical in every respect with that obtained by the bromination method, and a mixture of the two melted at 223°:

0·4666, by Kjeldahl's method, required 15·5 c.c. N/10-HCl. N=4·64.  
0·4104 gave 0·2540 AgBr. Br=26·34.

$C_{11}H_{10}O_2NBr$  requires N=4·61; Br=26·31 per cent.

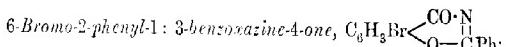


Two grams of 6-bromo-2-phenyldihydro-1:3-benzoxazine-4-one in 30 grams of pyridine were shaken with 20 c.c. of 10 per cent. sodium hydroxide for half an hour, after which time the bright yellow colour first produced had disappeared. The solution was diluted with water to 750 c.c., and acidified at 0° with dilute hydrochloric acid. The resulting thick, white, amorphous precipitate, consisting of the *syn*-bromo-derivative, was collected, repeatedly washed with water, and dried on porous porcelain in a vacuum. The melting point (100—150°) was indefinite, and it was not found possible to crystallise the compound without rearrangement to the cyclic isomeride, but it was practically pure, as shown by its properties and analysis. The yield was quantitative:

0·5166, by Kjeldahl's method, required 17·2 c.c. N/10-HCl. N=4·66.  
0·4952 gave 0·1238 AgBr. Br=26·67.

$C_{11}H_{10}O_2NBr$  requires N=4·61; Br=26·31 per cent.

*syn-Benzylidene-5-bromosalicylamide* is very sparingly soluble in solvents in the cold, whilst in the hot it rearranges. On melting, it also rearranges in the course of about forty-five seconds to 6-bromo-2-phenyldihydro-1:3-benzoxazine-4-one, which solidifies in the tube, and then melts at 219—220°.



#### 1. Preparation from 6-Bromo-2-phenyldihydro-1:3-benzoxazine-4-one.

The action of bromine on 6-bromo-2-phenyldihydro-1:3-benzoxazine-4-one was examined under a variety of conditions, but in

no case could the desired 6-bromo-2-phenyl-1:3-benzoxazine-4-one be isolated. The action in all cases led to fission of the ring, with production of 5-bromosalicylamide. Chlorine, however, gave the desired result. Eight grams of 6-bromo-2-phenyldihydro-1:3-benzoxazine-4-one, dissolved in the minimum quantity of benzotrichloride at 110°, were treated with a rapid current of dry chlorine for one hour. On cooling, a mass of fine needles separated, consisting of 6-bromo-2-phenyl-1:3-benzoxazine-4-one, which, after washing with benzene, melted at 202°, and on recrystallisation from benzene at 207°. The yield was 5 grams, and the product was identical in all respects with that obtained by method 2 (see below): 0·4078, by Kjeldahl's method, required 13·7 c.c.  $N/10\text{-HCl}$ .  $N = 4\cdot07$ . 0·4022 gave 0·2522 AgBr.  $\text{Br} = 26\cdot68$ .  $\text{C}_{14}\text{H}_8\text{O}_2\text{NBr}$  requires  $N = 4\cdot64$ ;  $\text{Br} = 26\cdot50$  per cent.

## 2. Preparation from O-Benzoyl-5-bromosalicylamide.

The method employed was similar to that adopted by Titherley (Trans., 1910, 97, 208), using anisole as a solvent. A very slow stream of dry hydrogen chloride was passed into a solution of 2 grams of O-benzoyl-5-bromosalicylamide (p. 28) in 10 c.c. of anisole at 150° contained in a small distilling flask. The anisole slowly distilled off, carrying with it the water formed in the reaction. The resulting yellow syrup, which solidified on cooling, was digested with 50 c.c. of dry boiling benzene. This left a quantity of N-benzoyl-5-bromosalicylamide (0·2 gram), and the filtrate, on cooling, deposited 6-bromo-2-phenyl-1:3-benzoxazine-4-one in a practically pure condition (1 gram), melting at 207°. On recrystallisation from benzene, it was obtained in small, white needles, melting at 208°:

0·1770, by Kjeldahl's method, required 6·0 c.c.  $N/10\text{-HCl}$ .  $N = 4\cdot75$ . 0·1330 gave 0·0814 AgBr.  $\text{Br} = 26\cdot04$ .

$\text{C}_{14}\text{H}_8\text{O}_2\text{NBr}$  requires  $N = 4\cdot64$ ;  $\text{Br} = 26\cdot50$  per cent.

The compound is sparingly soluble in cold alcohol, acetone, or benzene, but readily so in the hot solvents, and it is moderately soluble in cold chloroform. It is not acted on by cold dilute sodium hydroxide, but with strong aqueous or alcoholic ammonia it gives bright orange needles like the corresponding chloro-derivative. Dilute acids in the cold do not affect the bromo-derivative, but in hot alcoholic solution the ring undergoes disruption with addition of water, yielding N-benzoyl-5-bromosalicylamide (m. p. 240°), which separates as a voluminous mass, the yield being quantitative. This N-benzoyl derivative was identical with the product obtained by the rearrangement of O-benzoyl-5-bromosalicylamide (p. 28), and a

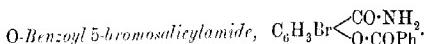
## 28 6-BROMO-2-PHENYLDIHYDRO-1:3-BENZOXAZINE-4-ONE.

mixture of the two melted at 240°. It gave the following figures on analysis:

0·3648, by Kjeldahl's method, required 11·5 c.c. N/10-HCl. N = 4·41.

0·1810 gave 0·1080 AgBr. Br = 25·53.

$C_{14}H_{10}O_2NBr$  requires N = 4·38; Br = 25·00 per cent.



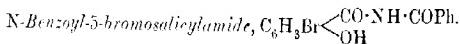
A solution of 10 grams of 5-bromosalicylamide in 40 grams of pyridine (dried over barium oxide) was treated with 10 grams of benzoyl chloride with continued shaking. The temperature was kept at -15° during the addition, which occupied one and a-half hours, and the resulting bright red mixture was kept at -15° for a further hour. It was then treated with 50 c.c. of dry ether, the ethereal pyridine solution decanted off, and the yellow, solid mass treated with dilute sulphuric acid at 0°. An insoluble buff powder remained, consisting of the crude O-benzoyl derivative, which, after washing with water and ether, weighed 10 grams. On recrystallisation from boiling toluene, it separated in fine, colourless, glistening needles, melting at 154°:

0·6488, by Kjeldahl's method, required 20·3 c.c. N/10-HCl. N = 4·38.  
0·4528 gave 0·2620 AgBr. Br = 24·73.

$C_{14}H_{10}O_2NBr$  requires N = 4·38; Br = 25·00 per cent.

O-Benzoyl-5-bromosalicylamide is sparingly soluble in the usual solvents. In boiling alcohol it dissolves, but almost immediately rearranges to the N-benzoyl isomeride (m. p. 238°), which separates on cooling slightly.

The same rearrangement occurs on melting, the liquid at 154° setting in about forty-five seconds to the solid N-benzoyl derivative, which then melts at 240°.



Two grams of O-benzoyl-5-bromosalicylamide were dissolved in the least possible quantity of boiling alcohol, and the solution diluted to 200 c.c. with water at 80°. The temperature was then kept at the boiling point for a few minutes, when a thick, curdy precipitate of the pure N-benzoyl derivative, melting at 248°, was obtained. On recrystallisation from pure acetic acid, the melting point was raised to 249°:

0·4526, by Kjeldahl's method, required 14·2 c.c. N/10-HCl. N = 4·39.  
0·3142 gave 0·1842 AgBr. Br = 24·95.

$C_{14}H_{10}O_2NBr$  requires N = 4·38; Br = 25·00 per cent.

*N-Benzoyl-5-bromosalicylamide* is very sparingly soluble in all the usual solvents, hot or cold. It may, however, be recrystallised from acetic acid if the operation be carried out fairly rapidly to avoid rearrangement. It gives intense yellow sodium and ammonium salts, which are sparingly soluble in water, from which, on acidification, the substance is precipitated in a colourless, gelatinous form.

*Rearrangement.*—One gram of the *N*-benzoyl derivative was boiled with 25 c.c. of glacial acetic acid for four hours. On cooling, 0·2 gram of unchanged substance separated out, and on diluting the filtrate with water, 0·5 gram of *O*-benzoyl-5-bromosalicylamide was obtained (m. p. 150°), which, on recrystallisation from toluene, melted at 154°. It was completely identical in all its properties with the synthetic product.

ORGANIC LABORATORY,  
UNIVERSITY OF LIVERPOOL.

#### IV.—*Synthesis of Camphoric Acid.*

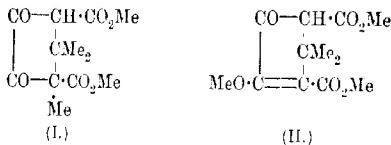
By GUSTAV KOMPPA.

A RECENT paper published simultaneously by G. L. Blanc and J. F. Thorpe in France (*Bull. Soc. chim.*, 1910, [iv], 7, 740) and England (*Trans.*, 1910, **97**, 836), throwing doubt on my synthesis of camphoric acid, suggests that I could never have obtained that substance by the process described, and that my conclusions are based on an error. Although in a position to reply immediately to these critics, I thought it desirable first to make some complementary experiments, and at the same time possibly to show that Blanc and Thorpe are themselves mistaken in drawing somewhat hasty conclusions from their incomplete treatment of the subject. In this I have now succeeded, and the present communication is my reply to their arguments.

In the first place, the above mentioned investigators declare that the basis of my synthesis, methyl diketo-*apo*-camphorate, cannot be produced in sufficient quantities (J. F. Thorpe, *Proc.*, 1909, **25**, 94; G. L. Blanc, *Bull. Soc. chim.*, 1909, [iv], **5**, xvi). Blanc even goes so far as to say in his address, "Le Camphre," delivered before the Société Chimique, "qu'il lui a été personnellement impossible de reproduire" this substance, and that the reaction according to which it was obtained "sur le papier ne présente pas grande chance de réussite." When I published a complete account of my researches, including the method of preparing the substance, they were able

to make use of the latter for their own experiments; they found it had the properties which I had previously described, although the yield which they obtained was not so good as it might have been according to my prescription. It is unnecessary to dispute this point, however, because it is not easy for a worker unfamiliar with this reaction to arrive at satisfactory results, towards the attainment of which I have been compelled to persevere for years. Nevertheless, my assistants, on becoming accustomed to the task, have usually been successful. For example, Mr. A. Lampén's yield varies from 45 to 70.5 per cent., Mr. B. Ingman's from 49 to 67 per cent., and Mr. W. Salvén's from 45 to 70 per cent., all being calculated as described in my paper. With the best intentions, it is not always possible to give a sufficiently detailed description of such a difficult and complicated method of preparation, and the yield may be affected by some condition as yet unknown; but I have had in my possession several hundred grams of methyl diketo-*apocamphorate*.

The product obtained by Blanc and Thorpe on methylating this diketo-ester by my process was identical with mine, the melting point being 85—88°. In their last paper, these chemists argue that the methyl derivative is not, as I supposed, the *C*-methyl derivative (I), but the *O*-methyl ether (II):



This they claim to have proved by treating the methyl derivative melting at 85—88° with potassium hydroxide, obtaining an amount of potassium derivative corresponding with 50 per cent. of methyl diketo-*apocamphorate*, and isolating from the mother liquor 40 per cent. of  $\beta\beta$ -dimethylglutaric acid without detecting  $\alpha\beta\beta$ -trimethylglutaric acid; according to this result, the methyl group in the diketo-ester melting at 85—88° is eliminated by alkali. On the supposition that the methyl group is not attached to carbon, they argue that I could not have obtained camphoric acid from the ester melting at 85—88°, and that my report is based on "an error." They have made this statement without having even tried to reduce the substance according to my directions. They do not even seek to explain what kind of error underlies my conclusions.

In considering whether a mistake has possibly been made, it is necessary to point out that if the methyl group were attached to oxygen instead of to carbon, reduction would lead to *apocamphoric*

acid as the final product. This melts at about the same temperature as *r*-camphoric acid, and although the appearance of the two substances under a microscope is not exactly similar, yet confusion is possible. But mixing together *apocamphoric* and *r*-camphoric acids causes a depression of 15–16° in the melting point, whereas the saturated acid which I obtained from the ester melting at 85–88° does not in the least depress the melting point of natural *r*-camphoric acid. Moreover, there is a difference of 45° in the melting points of the anhydrides of *apocamphoric* and camphoric acids. This fact, taken in conjunction with the dissimilar appearance, renders it impossible for any chemist to make such a mistake. Furthermore, I have not only synthesised *r*-camphoric acid and its anhydride, but also *r*-*isocamphoric* acid and *r*-dehydrocamphoric acid, which synthetical acids I have compared directly with the corresponding acids prepared from natural sources, demonstrating that these, when mixed together, do not effect a depression in the melting point, and that they are also in other respects identical. I attach a special significance to the identity of synthetic dehydrocamphoric acid with *r*-dehydrocamphoric acid prepared from *r*-camphoric acid. In 1903 I described the properties of dehydrocamphoric acid (*Ber.*, 1903, **36**, 4334), obtained synthetically from the ester melting at 85–88°, whilst only two years ago I procured this acid from natural *r*-camphoric acid, and showed that they were identical (*Annalen*, 1909, **370**, 212). That this synthetical dehydro-acid cannot be the corresponding dehydro*apocamphoric* acid is clear also from the fact that the two acids, although having the same melting point, cause a depression of 14° when mixed together.

Even yet the facts are not all disclosed, but the foregoing is sufficient evidence that an earnest chemist could not possibly commit an error such as Blanc and Thorpe would suggest, and that the experimental results, as I have stated them to be, can be established.

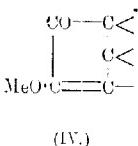
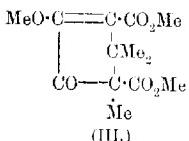
In his quoted paper, Thorpe lays special stress on the passage: "It was from the pure crystalline material that Komppa prepared camphoric acid." As it appears from my laboratory notes that the methyl diketocamphorate used for my synthesis had been crystallised once only, I deemed it important to show that the camphoric acid I obtained could not have arisen from any possible impurities in the diketo-ester. Accordingly, with the assistance of Dr. O. Routala, I have again prepared a thoroughly purified ester melting at 85–88°, and reduced it, first with sodium amalgam and then with hydrogen iodide, precisely as was stated in my complete report (*Annalen*, 1909, **370**, 209), obtaining once more the same yield of the same dehydro-acid, melting at 223–224° (normal thermometer);

the product, when mixed with *r*-dehydrocamphoric acid, again failed to cause depression of the melting point. This is the fifth occasion on which, with the aid of three different assistants, I have completely synthesised the acid; as it is identical with *r*-dehydrocamphoric acid prepared from *r*-camphor, and as I have also three times, with two different assistants, changed this synthetical dehydro-acid into *r*-camphoric acid and also into *isocamphoric acid*, it seems to me wholly impossible that other chemists should fail to prepare camphoric acid from the same substance.

But how is it to be explained that Blanc and Thorpe have not even tried to reduce the substance melting at 85—88°, in order to ascertain whether they could obtain camphoric acid or dehydro-camphoric acid according to my method? It is evident from the discussion following Thorpe's paper that the reason for this neglect was the supposition that, because the methyl group is removed by alkali from the ester melting at 85—88°, it is also removed by reducing, according to my prescription, with sodium amalgam followed by hydriodic acid. Here they have made the serious mistake of not taking into account the fact that I do not reduce in caustic alkali solution, but in alkali carbonate, or rather in alkali bicarbonate, a rapid stream of carbon dioxide being led, during the whole operation, through the reducing solution. That sodium carbonate does not eliminate the methyl group from the substance melting at 85—88° must be known to them, because in preparing the latter according to my method they separated it from the neutral product of methylation by extracting it several times with sodium carbonate solution, and isolating the ester by acidifying this liquid. It would surely have been worth while to reduce the ester in question by my process, even if the methyl group is eliminated by caustic alkali, a point which I have not yet had time to verify.

I do not, however, admit that the ester melting at 85—88° is the *O*-methyl derivative (II), as claimed by Blanc and Thorpe on account of its behaviour towards alkali, because camphoric and dehydrocamphoric acids can be synthesised from it. That this ester is, as I have supposed from the outset, the *C*-methyl derivative is demonstrated in the following manner. The ester in question produces, in common with all  $\alpha$ -diketones, a yellowish-brown colouring matter (quinoxaline), which has a strong green fluorescence when dissolved in ether and in alcohol, developing with mineral acids a dark red coloration destroyed by water, properties which characterise quinoxalines. I have not succeeded in crystallising this colouring matter, or the one from *o*-tolylenediamine, and have therefore not been able to analyse it. When one takes into account the fact that the neutral ether, obtained by methylating diketo-

*apocamphoric ester*, and to which I have ascribed the following constitution (III):



does not give the above-mentioned fluorescence, although it contains the same grouping of elements (IV) which Blanc and Thorpe suppose to exist in the ester melting at 85—88°, the coloration observed is not to be ignored. The difference in constitution between the ester melting at 85—88° and the neutral ester (III) is indicated more plainly when phenylenediamine hydrochloride is used instead of the free base. With this agent, the ester melting at 85—88° develops a red coloration at the ordinary temperature, and slight heating produces the effect very easily, this intense red solution not being given by the neutral ester (III). Attempts to produce osazones from the ester melting at 85—88° have led to oils, which have not been investigated further.

The constitutional formulae which I have ascribed to these substances are confirmed by the following determinations of the methoxy-group according to Zeisel's method:

0·2500 (ester m. p. 85—88°) gave 0·4495 AgI. MeO = 23·74.

0·2000 " " 0·3620 AgI. MeO = 23·89.

Formula I requires 24·22; formula II requires 36·33 per cent.

0·2106 (neutral ether) gave 0·5223 AgI. MeO = 32·76.

Formula III requires 34·44 per cent.

As the methyl group in the ester melting at 85—88° is not removed by boiling hydriodic acid, it is certainly not attached to oxygen, as suggested by Blanc and Thorpe, thus indicating the constitution (formula I) which I have already advocated, namely, that of diketocamphoric ester.

From all these facts, it is evident that the criticisms of my camphoric acid synthesis put forward by Blanc and Thorpe are completely baseless.

CHEMICAL LABORATORY,  
INSTITUTE OF TECHNOLOGY,  
HELSINKI, FINLAND.

V.—*Hydroxycodeine: a New Alkaloid from Opium.*

By JAMES JOHNSTON DOBBIE and ALEXANDER LAUDER.

THE new opium alkaloid, which forms the subject of this communication, was discovered by Messrs. T. and H. Smith, of Edinburgh, who were good enough to place a small quantity of the hydrobromide in our hands for investigation. The alkaloid is found in very small quantity in the last mother liquors obtained in the working up of the opium alkaloids, after all the other alkaloids have been eliminated.

The alkaloid is readily soluble in water, alcohol, ether, chloroform, benzene, or anil alcohol, but, so far, has not been obtained in a crystalline condition. From all these solvents it separates in the form of a varnish. The alkaloid has no definite melting point; on heating, it begins to soften about 40°, and is completely melted at 51°.

Of the common salts, the *hydrobromide* and the *hydrochloride* both crystallise well; the hydrobromide is, however, much less soluble than the hydrochloride, and it was therefore selected for analysis. It readily crystallises from water in large, hard, prismatic crystals, which contain no water of crystallisation. The crystals were dried at 100°, and gave the following results on analysis:

0·3341 gave 0·6678 CO<sub>2</sub> and 0·1808 H<sub>2</sub>O. C=51·46; H=6·00.

0·3318 „ 0·6614 CO<sub>2</sub> „ 0·1680 H<sub>2</sub>O. C=54·36; H=5·62.

0·4502 „ 11 c.c. N<sub>2</sub> (moist) at 17° and 742 mm. N=3·52.

0·2988 „ 9 c.c. N<sub>2</sub> (moist) „ 14·4° and 754 mm. N=3·50.

0·6056 „ 0·284 AgBr. Br=19·95.

0·5210 „ 0·244 AgBr. Br=19·92.

Mean, C=54·41; H=5·81; N=3·51; Br=19·94.

C<sub>18</sub>H<sub>21</sub>O<sub>4</sub>N.HBr requires 54·54; H=5·55; N=3·53;

Br=20·20 per cent.

*Platinichloride.*—The alkaloid was dissolved in dilute hydrochloric acid, and precipitated with excess of platinum chloride; the precipitate was well washed, and dried at 100° for analysis:

0·3258 gave 0·4942 CO<sub>2</sub> and 0·1296 H<sub>2</sub>O. C=41·36; H=4·42.

0·2452 „ 0·3725 CO<sub>2</sub> „ 0·0975 H<sub>2</sub>O. C=41·43; H=4·41.

0·2744 „ 7 c.c. N<sub>2</sub> (moist) at 14° and 755 mm. N=2·98.

0·1768 „ 0·0328 Pt. Pt=18·55.

0·2764 „ 0·2280 AgCl. Cl=20·39.

(C<sub>18</sub>H<sub>21</sub>O<sub>4</sub>N)<sub>2</sub>H<sub>2</sub>PtCl<sub>6</sub> requires C=41·54; H=4·23; N=2·69;

Pt=18·75; Cl=20·48 per cent.

*Determination of Methoxy Groups.*—The number of methoxy groups was determined by Zeisel's method:

0·4052 gave 0·2408 AgI. OMe=7·82.

0·3426 , , 0·2064 AgI. OMe=7·93.

OMe·C<sub>17</sub>H<sub>18</sub>O<sub>3</sub>N·HBr requires OMe=7·83 per cent.

*Methiodide*.—The methiodide was prepared by dissolving a small quantity of the alkaloid in a mixture of methyl iodide and methyl alcohol. The methiodide separated in colourless plates. It was recrystallised from methyl alcohol, and dried over sulphuric acid:

0·2076 gave 0·1098 AgI. I=28·57.

C<sub>15</sub>H<sub>21</sub>O<sub>4</sub>NI requires I=27·79 per cent.

This result is sufficient to show that the alkaloid is a tertiary base.

*Specific Rotation*.—An aqueous solution of the hydrobromide is slightly dextrorotatory:

I. 5·1884, in 100 of water, gave, in a 1-dm. tube at 20°,  $\alpha_1^{20} +0·9^{\circ}$ ; D<sub>4</sub><sup>20</sup> 1·0158; whence  $[\alpha]_D^{20} +17·07^{\circ}$ .

II. 5·0741, in 100 of water, gave, in a 1-dm. tube at 20°,  $\alpha_1^{20} +0·9^{\circ}$ ; D<sub>4</sub><sup>20</sup> 1·0154; whence  $[\alpha]_D^{20} +17·4^{\circ}$ .

*Colour Reactions*.—With Fröhde's reagent, the new alkaloid gives a yellowish-green colour, which gradually changes to blue; and with Mandelin's reagent a yellowish-green, also changing to blue on keeping. These reactions are practically identical with those given by codeine with the same reagents.

*Absorption Spectra*.—The absorption spectra of an aqueous solution of the hydrobromide were photographed. The spectra show a well-marked absorption band at 1/λ 3500. The position of this band is identical with that of codeine (Hartley, *Phil. Trans.*, 1885, Part II, 471; Dobbie and Lauder, *Trans.*, 1903, **83**, 605), but the codeine band is very slightly more persistent.

The discoverers propose the name *neopine* for the new alkaloid. Although, owing to the small quantity of material at our disposal, the chemical evidence is still incomplete, the alkaloid is almost certainly a hydroxycodeine, but it is not identical with the hydroxycodeine prepared by Ach and Knorr (*Ber.*, 1903, **36**, 3067) by the oxidation of codeine. Its formula differs from that of codeine only in the possession of an additional atom of oxygen, which, owing to the solubility, is probably present in an hydroxyl group. Like codeine, it contains only one methoxyl group. Further evidence of the close relation between the two alkaloids is afforded by the practical identity of their absorption spectra.

The physiological action of the new alkaloid has been investigated by Professor Stockman, of Glasgow University.

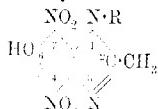
THE GOVERNMENT  
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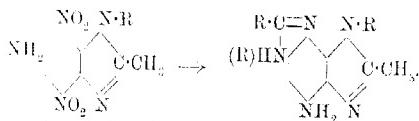
VI.—*Syntheses with Phenol Derivatives Containing a Mobile Nitro-group. Part III. Complex Iminazoles, Azo-compounds, and Azides.*

By RAPHAEL MELDOLA and HAROLD KUNTZEN.

The extreme mobility of the 3-nitro-group in 2:3:5-trinitro-4-acetylaminophenol when the latter compound is allowed to interact with primary amines has been taken advantage of for the synthesis of iminazoles and other compounds and for the study of the influence of the position of substituents in determining the yield of iminazole, etc. (Trans., 1906, **89**, 1935; 1908, **93**, 1659; 1909, **95**, 1033). The object of the present extension of the research was, in the first place, to ascertain whether complex iminazoles containing two iminazole rings attached to one benzene nucleus were capable of existence. Although the results in this direction have not hitherto been promising, we think it desirable to place upon record the principle which has been adopted, because we propose continuing the experiments in this direction. It will be seen from the general formula of the iminazoles synthesised by this method:



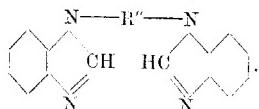
that there are two groups in the benzene ring which might, under suitable treatment, be made to furnish the iminazole ring, namely, the 6-hydroxy- and 7-nitro-group. If, by the action of ammonia or amines on the iminazoles or their ethers (Trans., 1908, **93**, 1672, etc.), an amino-group or substituted amino-group could be substituted for the 6-hydroxyl group, dinitro-derivatives would be formed, which, on acylation and reduction, might be expected to furnish compounds of the type of the hitherto unknown benzodiminoazoles:



Many experiments have been made with the methyl ether of the iminazole from aniline and the trinitro-compound, but the difficulty appears to be the initial step of substituting the amine residue for the 6-hydroxy-group. It is well known, however, that the mobility

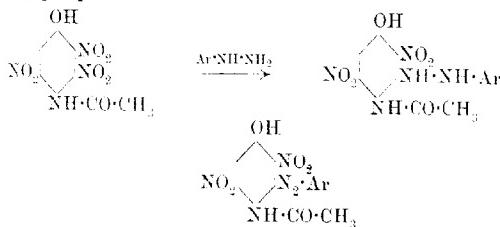
of the alkyloxy-group increases with the weight of the radicle attached to the oxygen atom, and the experiments will be continued with ethers containing the higher homologues of methyl.

The other direction in which the research has been pursued had also for its object the synthesis of compounds containing two iminazole rings, but linked by a bivalent radicle. Compounds of this type would differ from the foregoing benzdi-iminazoles, and might be termed bisiminazoles. The type would be:



As will be seen from the experimental section of this paper, a compound of this type has been prepared, but owing to its colloidal character and the difficulty of obtaining any definite crystalline derivatives, it has not been found possible to characterise the pure substance.

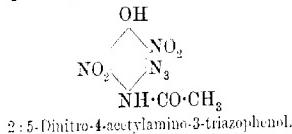
The formation of azo-derivatives by the interaction of the trinitro-compound and hydrazines was indicated in a former paper (Trans., 1946, **89**, 1943). This new synthesis of azo-compounds by direct substitution in the benzene nucleus has been further studied, and the conditions which favour the maximum yield have been experimentally ascertained. In this reaction, an intermediate hydrazo-compound is formed by catenation, and from the latter the azo-compound is formed by the oxidising action of the eliminated nitro-group:



In connexion with this synthesis, it has been discovered that secondary hydrazines of the types:  $\text{Ar}_2\text{N} \cdot \text{NH}_2$ ,  $\text{ArRN} \cdot \text{NH}_2$  do not form azo-compounds, whereas all primary hydrazines readily undergo condensation with the trinitro-compound. Thus, phenyl-, tolyl-, and nitrophenyl-azo-compounds are readily obtained from the trinitro-compound and the respective hydrazines, whilst phenylmethylhydrazine and diphenylhydrazine give only resinous products, arising partly from the breaking down of the trinitro-compound, and

partly, from the decomposition of the hydrazine by the eliminated nitro-group.

Another synthesis made possible through the mobility of the 3-nitro-group is that of azides (triazole-compounds), the trinitro compound reacting readily with sodium azide to form the compound:



The other product of the reaction is sodium nitrite.

#### EXPERIMENTAL.

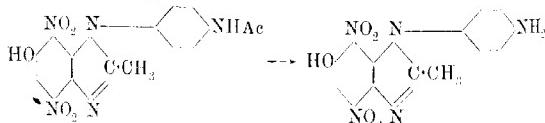
##### *The Iminazole from the Trinitro-compound and Acetyl-p-phenylenediamine.*

As the trinitro-compound does not give the aminoinimazole required as an intermediate product by interaction with *p*-phenylenediamine (Trans., 1909, **95**, 1033), the acetyl derivative of the latter was made use of. The trinitro-compound and three molecular proportions of acetyl-*p*-phenylenediamine were boiled together in alcoholic solution for two hours, the product was extracted by dilute hydrochloric acid, and purified by alternate alkaline and acid treatment in the way described in connexion with all the other iminazoles synthesised by our method. Two grams of trinitro compound gave 2·13 grams of iminazole. *4 : 7-Dinitro-6-hydroxy-1-p-acetylaminophenyl-2-methylbenziminazole* crystallises from alcohol, in which it is very sparingly soluble, in dense, ochreous scales, melting at 261·5°:

0·0722 gave 11·9 c.c. N<sub>2</sub> (moist) at 15° and 742·4 mm. N = 18·85.  
 $\text{C}_{16}\text{H}_{13}\text{O}_6\text{N}_5$  requires N = 18·87 per cent.

##### *Hydrolysis of the Acetylaminoinimazole.*

The removal of the acetyl group and the purification of the resulting aminoiminazole has proved a task of the greatest difficulty, and numerous unsuccessful experiments were carried out before the required compound was obtained. The synthesis which had to be realised is shown by the formulae:



Alkaline hydrolysists are ineffective, and after many trials it was found that strong sulphuric acid was the best hydrolysing agent for the purpose. The acetyl derivative is not basic, but dissolves in cold concentrated sulphuric acid, and is precipitated on dilution with water. In order to effect the hydrolysis, the acetyl derivative is dissolved in concentrated sulphuric acid, a little water added (not enough to precipitate the substance), and the solution heated until a drop remains clear on dilution with water, thereby showing that the basic aminoiminazole has been formed. If the sulphuric acid is too strong or the temperature raised above the point at which hydrolysis is shown to have taken place by the test described, complete decomposition ensues, and the materials are lost. After hydrolysis, the solution is diluted with water, filtered, if necessary, and exactly neutralised with ammonia. The precipitate is collected, washed, and purified by solution in dilute hydrochloric acid, filtering, and reprecipitating with ammonia. This treatment is necessary, because some of the acetyl derivative escapes hydrolysis, and on dilution and neutralisation the precipitate appears to contain, not only the required basic amino-compound, but also a salt of the latter with the unchanged acid acetyl derivative. It is unsafe to carry the hydrolysis to the extreme point on account of the tendency to undergo decomposition.

The purification of the aminoiminazole after separation from the unchanged acetyl derivative presented great difficulties on account of the combined phenolic and basic character of the molecule. The compound forms salts with both acids and bases, so that some difficulty was experienced in preparing a pure specimen for analysis. After many trials, it was found that the compound formed an ammonium salt, which crystallised from water in stumpy, dull orange needles:

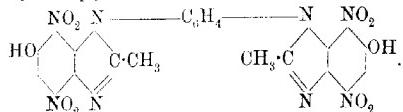
0.0756 gave 15.6 c.c.  $N_2$  (moist) at  $16^\circ$  and 768 mm.  $N = 23.99$ .  
 $C_{14}H_{14}O_5N_6$  requires  $N = 24.28$  per cent.

This ammonium salt, when dissolved in water and decomposed by exact neutralisation with dilute hydrochloric acid, gives the free 4:7-dinitro-6-hydroxy-1-p-aminophenyl-2-methylbenzimidazole as an ochreous, microcrystalline powder, very sparingly soluble in boiling alcohol, and separating from the latter solvent in ochreous nodules, having no definite melting point, but decomposing with charring from about  $215^\circ$ :

0.1800 gave 32.5 c.c.  $N_2$  (moist) at  $18.5^\circ$  and 756.5 mm.  $N = 20.7$ .  
 $C_{14}H_{14}O_5N_5$  requires  $N = 21.21$  per cent.

On account of the difficulty of crystallising the substance, no further purification was attempted, but the product was acted on by trinitro-compound, as described below.

*Synthesis of the Bisiminazole: 4: 4': 7: 7'-Tetranitro-6: 6'-di-hydroxy-1: 1'-p-phenylene-2: 2'-dimethylbisbenzimidazole.*



The aminobenzimidazole obtained as above was boiled in alcoholic solution with trinitro-compound in the proportion of one molecule of the latter to two of the former, and the ochreous granular substance, which separated in the course of two or three hours, was submitted to the acid and alkaline treatment generally adopted. There is no doubt that the product is the bisiminazole required, but it was found impossible to crystallise it from any solvent, and no specimen pure enough for analysis could be obtained. The compound is extremely insoluble in all the usual organic solvents, and the minute quantity which does dissolve separates out in a colloidal state on cooling. It is phenolic in character, dissolving in dilute alkalis with an orange colour, and being precipitated by acids as a brown, gelatinous mass, which dries to a brittle, brown resin. On adding silver nitrate to a solution of the ammonium salt, a brown, gelatinous, insoluble silver salt is precipitated, and this also dries to a brown resin. Analyses of this resin gave:

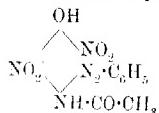
Found, Ag = 27.74 and 29.43.

$C_{22}H_{12}O_4N_4Ag_2$  requires Ag = 28.26 per cent.

The general properties of this new type of substituted bis-imidazoles are not such as to encourage a further detailed study of the compound. The existence of the type having, however, been established, we propose extending the research with a view to preparing the isomeride containing the *m*-phenylene nucleus, in the hope that this compound may be more amenable to treatment by ordinary chemical methods.

#### *Synthesis of Azo-compounds.*

3-Benzeneazo-2: 5-dinitro-4-acetylaminophenol,



has already been described (Trans., 1906, **89**, 1943) in a preliminary way, and a further study of the compound now enables us to give more complete and more correct details concerning its mode of

formation and properties. In the first place, we have found that in order to ensure the production of a pure compound, the trinitro-acetylaminophenol and phenylhydrazine must be allowed to interact only in equimolecular proportions. If excess of phenylhydrazine is present, some secondary reaction with the azo-compound takes place, and products arising from the reduction of the latter are formed. These impurities are extremely difficult to remove, and their association with the azo-compound tends to disguise the characters of the latter. Our first preparation of decomposing point 188° was no doubt contaminated to a sufficient extent to depress the decomposing point, as we now find that the pure compound decomposes at 248°.

In order to prepare the azo-compound, equimolecular proportions of the trinitro-compound and of phenylhydrazine are dissolved in a small quantity of alcohol, and the solution is warmed until the red crystalline salt, which at first separates out, passes into solution. When this stage has been reached it is better to remove the flask from the water-bath and to allow the reaction to complete itself at the ordinary temperature. In the course of twelve hours, the formation of the azo-compound is complete, and the crystalline deposit can be collected, washed with alcohol, and crystallised from boiling glacial acetic acid. From this solvent it separates in large, ruby-red prisms, with a slight metallic lustre. It is but very sparingly soluble in boiling alcohol, but dissolves more readily in boiling pentachlorethane, forming a red solution, from which scarlet needles separate on cooling. The specimen used for analysis was crystallised from glacial acetic acid:

0·1318 gave 0·2350 CO<sub>2</sub> and 0·040 H<sub>2</sub>O. C=48·62; H=3·37.  
0·0783 „, 13·8 c.c. N<sub>2</sub> (moist) at 17° and 761·5 mm. N=20·64.  
C<sub>11</sub>H<sub>11</sub>O<sub>6</sub>N<sub>5</sub> requires C=48·68; H=3·21; N=20·29 per cent.

The azo-compound dissolves in concentrated sulphuric acid with an orange colour, and is precipitated unchanged on dilution with water. Attempts to eliminate the acetyl group by acid and alkaline hydrolysks led to negative results, the compound either not being hydrolysed or else decomposing completely. The hydroxyl group confers phenolic characters on the compound, and it forms alkaline salts, which are completely insoluble in presence of the slightest excess of alkali. The sodium salt is of a deep violet colour, insoluble in cold water, and dissolving in hot water with a dull red colour. On the addition of acid, the azo-compound is precipitated from the hot aqueous solution of the sodium salt in the colloidal state.

The azo-compound can be acetylated by keeping it in acetic anhydride solution in the presence of a small quantity of concentrated sulphuric acid for several days. Specimens withdrawn

from time to time and analysed showed that the substitution of acetyl for the hydroxylic hydrogen takes place but slowly. The product, which is precipitated as a dark, ochreous, crystalline powder on diluting the solution with water, melts and decomposes at about 203°:

0·0671 gave 10·5 c.c. N<sub>2</sub> (moist) at 15·5° and 761·3 mm. N = 18·31.  
 $C_{16}H_{15}O_7N_5$  requires N = 18·09 per cent.

This *acetyl* derivative decomposes on boiling with glacial acetic acid, with the evolution of nitrous fumes and the formation of some insoluble resinous product, together with a definite compound which crystallises out from the solution, on cooling, in ochreous needles. The latter, by repeated crystallisation from glacial acetic acid, were finally obtained with a definite decomposing point of 284—285°, and containing nearly the same percentage of nitrogen (18·2 and 18·01) as the original acetyl derivative, but less carbon. This product of decomposition appears to be of interest, but we have not yet been able to determine its constitution, and its study will be resumed.

#### 3-p-Nitrobenzeneazo-2: 5-dinitro-4-acetylaminophenol.

In order to prepare this compound, *p*-nitrophenylhydrazine and trinitroacetylaminophenol are dissolved in a small quantity of alcohol, the hydrazine being in slight excess of the quantity calculated for one molecular proportion of each compound. The solution is kept warm on the water-bath for an hour, care being taken to prevent actual boiling. On removing from the source of heat, and allowing to remain for some hours, the azo-compound separates out in crystalline nodules, which can be purified by washing with alcohol containing hydrochloric acid and crystallisation from glacial acetic acid. The compound dissolves in this last solvent with a deep orange colour, and separates, on cooling, in dark brown, glistening prisms, which appear ruby-red by transmitted light. It melts and decomposes at 244—245°:

0·1308 gave 23·8 c.c. N<sub>2</sub> (moist) at 13·5° and 763·5 mm. N = 21·61.  
 $C_{14}H_{16}O_6N_6$  requires N = 21·55 per cent.

This azo-compound can also be acetylated by prolonged action of acetic anhydride in presence of a little concentrated sulphuric acid. After five days at the ordinary temperature, a *diacetyl* derivative is formed, which consists of an ochreous, crystalline powder, decomposing at 160—168°:

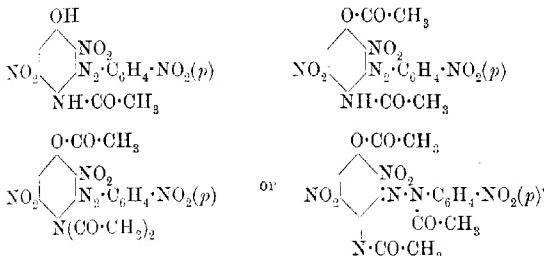
0·0744 gave 12·65 c.c. N<sub>2</sub> (moist) at 17° and 761·4 mm. N = 19·76.  
 $C_{16}H_{12}O_6N_6$  requires N = 19·45 per cent.

At the end of nine days under the same conditions, another acetyl

group is introduced, the resulting *triacetyl* derivative consisting of an ochreous, micro-crystalline powder, decomposing at 162–164°.

0·1226 gave 29·6 c.c. N<sub>2</sub> (moist) at 19·5° and 767·7 mm. N=17·57.  
C<sub>18</sub>H<sub>14</sub>O<sub>6</sub>N<sub>6</sub> requires N=17·73 per cent.

These acetyl derivatives are decomposed on boiling with glacial acetic acid, with the evolution of nitrous fumes and the formation of resinous products. As all the compounds described under this section are new, the formulæ are subjoined:



#### 2: 5-Dinitro-4-acetamino-3-triazophenol.

The trinitro-compound readily exchanges the 3-nitro-group for the triazo-group by interaction with sodium azide. A slightly warm aqueous solution of the latter is prepared, and to this the solid trinitro-compound is added in small portions. After some hours at the ordinary temperature, a crystalline deposit forms, and a further quantity of the triazo-compound is precipitated from the solution on acidifying with hydrochloric acid. The product, after being collected and washed with water, crystallises from alcohol in flat, ochreous needles or golden scales, melting at 167–168°:

0·1288 gave 32·5 c.c. N<sub>2</sub> (moist) at 15·3° and 765·9 mm. N=29·73.  
C<sub>8</sub>H<sub>6</sub>O<sub>6</sub>N<sub>6</sub> requires N=29·81 per cent.

The compound is phenolic in character, dissolving in alkalis with an orange colour and being reprecipitated by acids.

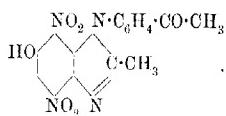
The triazo-compound could not be methylated either by methyl sulphate and alkali, or by silver oxide and methyl iodide. Attempts to remove the acetyl group by acid and alkaline hydrolysts led to negative results, the compound resisting hydrolysis or decomposing completely. Acetylation was effected in the usual way by means of acetic anhydride and sulphuric acid. After three days a product was obtained which, from the results of analysis, appeared to be a mixture of a *diacetyl* and a *triacetyl* derivative, and from

which, by repeated crystallisation from alcohol, the former was isolated in nodular tufts of yellow needles, melting at 140—141°;

0·0420 gave 9·3 c.c. N<sub>2</sub> (moist) at 17° and 759·2 mm. N = 25·66.  
C<sub>16</sub>H<sub>12</sub>O<sub>6</sub>N<sub>6</sub> requires N = 26·90 per cent.

On contact with dilute alkali the *O*-acetyl group is at once eliminated, and the original triazo-compound regenerated.

*The Iminazole from the Trinitro-compound and Aminoacetophenone: 4:7-Dinitro-6-hydroxy-1-p-acetylphenyl-2-methylbenzimidazole.*



This compound was prepared in the usual way by boiling an alcoholic solution containing the trinitro-compound and two molecular proportions of aminoacetophenone for about an hour, when the iminazole separates out in ochreous scales. Purification could not be effected in this case by the usual method of alkaline treatment, as the compound is resinified by the action of alkalis. After crystallisation from alcohol, in which it is but sparingly soluble, the compound consists of ochreous scales, melting somewhat vaguely with decomposition at 246°:

0·0624 gave 8·2 c.c. N<sub>2</sub> (moist) at 16·5° and 768 mm. N = 15·55.  
C<sub>16</sub>H<sub>12</sub>O<sub>6</sub>N<sub>4</sub> requires N = 15·74 per cent.

By the action of hydroxylamine acetate an *oxime* was obtained, which crystallised from alcohol in small, ochreous scales, melting at 223°;

0·0630 gave 10·3 c.c. N<sub>2</sub> (moist) at 13° at 754 mm. N = 19·16.  
C<sub>16</sub>H<sub>13</sub>O<sub>6</sub>N<sub>5</sub> requires N = 18·88 per cent.

The iminazole reacts also with phenylhydrazine, forming a *phenylhydrazone*, which crystallises from alcohol in ochreous nodules having a vague decomposing point of about 198°.

During much of this work we had the co-operation of Mr. J. Gordon Hay, to whom we desire to express our thanks.

FINSBURY TECHNICAL COLLEGE.

II.—*Investigations on the Dependence of Rotatory Power on Chemical Constitution. Part I. The Rotations of the Simplest Secondary Alcohols of the Fatty Series.*

By ROBERT HOWSON PICKARD and JOSEPH KEYNOR.

The authors hope to communicate to the Society a series of papers in which will be discussed the qualitative and quantitative dependence of rotatory power on chemical constitution, and feel it desirable to state at the outset their reasons for commencing yet a further investigation of this interesting problem.

It is obvious that in the present state of knowledge much of the previous work \* in this field is very difficult to correlate even in a qualitative manner. Now there are numerous investigations of the type, as, for example, (a) the very extended and careful researches of P. F. Frankland and his co-workers on the rotatory powers of derivatives of the optically active glyceric and tartaric acids; (b) the dependent work of Tschugaeff and of Rupe on the bornyl and menthyl esters of various acids, and (c) the paper of one of us and Littlebury on the esters of L-menthylicarbamic acid, in which in each case the effect of various substituents on the rotatory power of some optically active substance has been studied; that is to say, in the above instances the effect of substituting the alcoholic or carboxylic hydrogen atoms in glyceric and tartaric acids, in borneol, menthol, and menthylicarbamic acid. In the compounds described in such investigations the substituent is not attached to an asymmetric carbon atom, and is in many cases far removed from it in the molecule, whilst in several of the parent substances of such investigations there are more than one such carbon atom. It is thus often impossible to decide how far the effect of the substituent is due to its relative mass and how far to its structure, this particularly being the case in compounds containing the menthyl radicle (compare Pickard and Littlebury, Trans., 1907, 91, 301).

In addition to this difficulty there is also the additional one that it is often doubtful whether conclusions drawn from one group of comparatively complex compounds can be applied safely to those drawn from another group of widely differing constitution. Thus, for example, confusion may be introduced if the effect on the rotatory power of substituting the alcoholic hydrogen atoms be compared in such widely different compounds, as, for example, glyceric acid, menthol, or the

\* Up to the end of 1904 this is admirably summarised by Walden, *B.Z.*, 1905, 38, 345.

optically active amyl alcohol of fusel oil. Again, many of the compounds compared in such investigations are solids at the ordinary temperature, and the rotations of these have been determined in solution, although the effect of solvents on rotatory power is as yet little understood. Further, the effect of temperature on the rotatory powers of the pure liquids, considerable as it is in many cases, has been often disregarded, although in this respect the investigations of Frankland leave little to be desired.

These and similar difficulties are well exemplified when a comparison is made of the rotatory powers of the various compounds of  $\beta$ -phenyl propionic, cinnamic, and phenylpropionic acids which have been prepared by several investigators to show the relative effect of unsaturation on optical activity.

In table I will be found a list of the molecular rotatory powers of several of the compounds previously described, and also those of the esters of the three acids with *d*- and *l*-methyl-*n*-hexylcarbinol (Trans., 1907, 91, 2058). These esters of a simple secondary alcohol give results differing from those obtained with more complicated secondary alcohols, such as menthol and borneol.

TABLE I.

*Molecular Rotatory Powers of Esters and Salts of  $\beta$ -Phenylpropionic, Cinnamic, and Phenylpropionic Acids.*

Ester or Alkaloid.	Acid.		
	$\beta$ -Phenyl- propionic.	Cinnamic.	Phenyl- propionic
<i>l</i> -Amyl alcohol.	+ 5.0 <sup>a</sup>	+ 16.4 <sup>a</sup>	+ 12.4 <sup>a</sup>
(Methylhexylcarbinol)			
<i>l</i> -Menthol <sup>b</sup>	- 161.9	- 217.8	-
" <sup>c</sup>	178.3	235.5	+ 225.5
" <sup>d</sup>	171.5	171.6	165.7
" <sup>e</sup>	162.6	184.3	155.6
<i>d</i> -Borneol <sup>f</sup> <sup>g</sup>	+ 86.5	+ 82.5	+ 75.0
" <sup>h</sup>	82.9	82.6	80.7
<i>d</i> -Methyl- <i>n</i> -hexylcarbinol	+ 42.1	- 104.4	- 134.1
<i>l</i> -Methyl- <i>n</i> -hexylcarbinol	- 32.8	- 103.4	18.9 <sup>i</sup>
Ponitine <sup>j</sup>	- 5.1	- 29.6	- 19.7
Cinchonine <sup>k</sup>	+ 381.9	+ 475.2	+ 611.6

<sup>a</sup> Walden (*Zeitsch. physikal. Chem.*, 1896, **20**, 589). In the nomenclature of Marekwald (*Ber.*, 1902, **35**, 1549), this alcohol is *d*-amyl alcohol.

<sup>b</sup> Tschugaeff (*J. Russ. Phys. Chem. Soc.*, 1902, **34**, 606).

<sup>c</sup> Kupe (*Annales*, 1909, **369**, 311). Determinations in 10 per cent. benzene solution.

<sup>d</sup> Hilditch (Trans., 1908, **93**, 14). Determinations in 10 per cent. solution; (*i*) in chloroform, (*h*) in acetone.

The unsaturated esters have been quantitatively reduced to the saturated ester (see page 67).

<sup>e</sup> Hilditch (Trans., 1908, **93**, 713). Determinations in 4 per cent. chloroform solution.

These results (table I) show at once that no general conclusions can be drawn as to the quantitative effect on the rotatory powers of the alcohols and alkaloids named when the alcoholic hydrogen atom is displaced by acid radicles (or salts are formed with acids) of closely related constitution, but differing in the degree of unsaturation, for in some cases the ethylenic, and in the others the acetylenic, compound has the greater rotation.

It is, however, convenient at this juncture to recall that the vast amount of painstaking and laborious work in this field has led to certain well-founded, but very wide, generalisations. These need not now be re-stated, but are well exemplified by the investigations quoted in the table, which (with others) show that (we believe in every known case) the effect of unsaturation is exhibited in the exaltation of rotatory power.

Considerations such as these make the following conditions desirable for a re-investigation of this subject: (1) the active compounds compared should contain only one asymmetric carbon atom; (2) the effect of various radicles on the rotatory power should only be compared when these are attached directly to the asymmetric carbon atom, and (3) the compounds should be liquids and their rotatory powers should be measured in the pure state and at different temperatures.

Thus, whilst previous investigators have as a rule studied the variation in the rotatory power of some one compound caused by inactive substituents, the object of the present authors is to compare the rotatory powers of different series of comparatively simple compounds. Optically active compounds, however, of the type required are very little known, and it becomes therefore necessary to prepare them specially.

No class of compounds seems so likely as the alcohols to fulfil in general the third condition laid down, whilst the ease with which all types of alcohols can now be synthesised, thanks to the Grignard reaction and the catalytic reactions of the Toulouse school, makes this class of compounds particularly suitable for the purpose in view. Now one of us and Littlebury have described (Trans., 1907, 91, 1973) a method for what is believed to be the complete resolution of racemic alcohols, namely, by the fractional crystallisation of the salts formed by the combination of various optically active bases with the acid esters of the alcohol and a polybasic acid, whilst the present authors in a similar way carried out the first successful resolution (*loc. cit.*) of an aliphatic alcohol, namely, that of methyl-*n*-hexylcarbinol with  $[\alpha]_D \pm 99$ . The method has since been found to be a general one, and can be applied to several types of alcohols (see preliminary note, Proc., 1909, 25, 167); therefore, those types of alcohols which contain one asymmetric carbon atom, since they can be synthesised

and resolved into their optically active components, and since they have as a rule low melting points, appear to be very suitable for a re-investigation of the problem of the dependence of rotatory power on chemical constitution.

However, before describing the results obtained so far in this direction, attention should be called to the following evidence which will furnish an answer to the very obvious question as to whether such results might not be vitiated by an incomplete resolution of the racemic alcohols. Now, firstly, that the method has effected complete resolutions in some cases seem certain. For example, one of us and Littlebury (*loc. cit.*) prepared by this method four borneols, which all severally gave, when oxidised, camphors identical in rotatory power with the maximum exhibited by the natural products; thus the *d*-borneol and the *l*-isoborneol prepared each gave pure *d*-camphor, whilst the *l*-borneol and the *d*-isoborneol gave pure *l*-camphor. Again, the *d*-methyl-*n*-heptylcarbinol described below has an equal but opposite rotatory power to that of the specimen of the same compound isolated from oil of rue by Power and Lees \* (Trans., 1902, **81**, 152). Secondly, in the case of the fourteen alcohols, the resolutions of which are described below (with two exceptions),† there have been obtained either both the dextro- and laevo-rotatory forms of the alcohols with equal and opposite rotations, or both forms of the same acid ester with equal and opposite rotation, or two preparations of the same acid ester having identical rotations by fractional crystallisation of the salts of two different alkaloids or two preparations of the alcohol with identical positive rotation from two different acid esters. Thirdly, the recorded rotatory powers (see table II, p. 49) of the alcohols belonging to the same series show a gradual alteration as the series is ascended, and thus agree well one with the others. Fourthly, an exhaustive series of experiments failed to give any evidence against the optical purity of methyl-*n*-hexylcarbinol with  $[\alpha]_D^{25} \pm 9.4^\circ$ . In these, (a) the diethyl and dimethyl esters of *d*- and *l*-tartaric acid were allowed to remain in presence of hydrogen chloride with an excess or a deficiency of the *d*- or the *l*-alcohol, under which conditions the  $\beta$ -octyl group more or less completely displaces the methyl or ethyl group in the tartaric esters; (b) *d*- and *l*-tartaric acid were each treated in the same way with the two alcohols; (c) the  $\beta$ -octyl esters of the tartaric acids thus obtained were each hydrolysed partly with an insufficiency, or completely with an excess, of potassium hydroxide. In view of the experiments of Marckwald and McKenzie (*Ber.*, 1901,

\* *d*-Methyl-*n*-nonylcarbinol, as now obtained by synthesis, has a higher positive rotation than the laevo-rotatory alcohol isolated by these investigators from the same oil.

† Methyl-*n*-decyl- and phenylmethyl-carbinols.

34, 489) on the varying velocity of esterification of an optically active acid with the two optical isomerides of an alcohol and the varying rate of hydrolysis of the corresponding esters, it was to be expected that such experiments carried out under many varied conditions (including those detailed by them) would yield a product of rotatory power different from  $[\alpha]_D^{25} \pm 9.9^\circ$  if this were not the constant relating to optically pure methyl-*n*-hexylcarbinol. In no case, however, was a sample of the alcohol obtained as a result of these experiments of either lower or higher rotatory power.

#### *Resolution of Fourteen Alcohols.*

The resolution of fourteen alcohols is described in this section; twelve of these are of the general formula  $\text{CH}_3\cdot\text{CH}(\text{OH})\cdot\text{R}$ , where R represents the normal groups ethyl to undecyl, *isobutyl* and phenyl, whilst the other two have the formula  $\text{C}_2\text{H}_5\cdot\text{CH}(\text{OH})\cdot\text{R}'$ , where R' represents *n*-hexyl and phenyl. The preparation of these active alcohols has been repeated, and in all cases but two—methyl-*n*-decyl- and phenylmethyl-carbinol—the pure optically active alcohols have been obtained in at least two ways. In Figs.\* 1 and 2 is illustrated the variation of the specific rotations with the temperature, and table II shows how in the series methyl-*n*-propyl- to methyl-*n*-undecyl-carbinol the molecular rotatory powers tend to approach a common value. These resolutions have been carried out by the method described (*loc. cit.*) for methyl-*n*-hexylcarbinol, that is, by the fractional crystallisation from acetone or aqueous acetone of the alkaloidal salts of either the hydrogen phthalic or succinic esters. Where a

TABLE II.

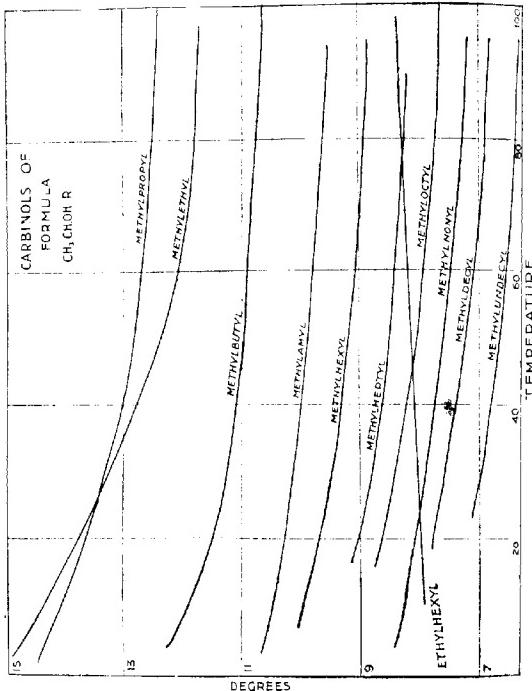
#### *Specific and Molecular Rotatory Powers of the Dextrorotatory Alcohols.*

Alcohol.	$[\alpha]_D^{20}$	$[\text{M}]_D^{20}$	$[\alpha]_D^{25}$	$[\text{M}]_D^{25}$	$[\alpha]_{D_2}^{20}$	$[\text{M}]_{D_2}^{20}$
Methylmethylecarbinol .....	+13.87*	+10.31	+12.48*	4.92*	+11.84*	+8.8*
Methyl- <i>n</i> -propylcarbinol... .	13.70	12.1	12.89	11.3	12.56	11.2
Methyl- <i>t</i> -butylcarbinol ...	11.57	11.8	11.92	11.2	10.90	11.1
Methyl- <i>n</i> -amylcarbinol ...	10.32	12.0	9.89	11.5	9.60	11.1
Methyl- <i>n</i> -hexylcarbinol ...	9.76	12.7	9.17	11.9	8.99	11.7
Methyl- <i>n</i> -heptylcarbinol...	8.49	12.9	8.55	12.3	8.30	12.0
Methyl- <i>n</i> -octylcarbinol ...	8.68	13.7	8.14	12.9	7.89	12.3
Methyl- <i>n</i> -nonylcarbinol ...	8.13	14.0	7.66	13.2	7.28	12.5
Methyl- <i>n</i> -decylcarbinol ...	7.73	14.5	7.27	13.5	6.89	12.8
Methyl- <i>n</i> -undecylcarbinol .	7.22	14.4	6.67	13.3	6.39	12.7
Methyl- <i>isobutyl</i> carbinol ...	20.54	20.9	19.25	19.6	18.32	18.7
Ethyl- <i>n</i> -hexylcarbinol .....	8.05	11.6	8.17	11.8	8.30	12.0
Phenylmethylecarbinol.....	42.86	52.3	42.68	52.1	41.60	50.8
Phenylethylecarbinol.....	27.73	37.7	32.52	44.2	35.51	48.3

\* It should be noted that in Fig. 2 the scale of the ordinates is one-third that of the scale of the ordinates in Fig. 1.

resolution was effected, in all cases brucine formed the least soluble salt (*IBdA*) with the dextrorotatory hydrogen phthalic esters and the dextrorotatory hydrogen succinic esters of the two alcohols containing the phenyl group, whilst with the purely aliphatic alcohols this alkaloid formed the least soluble salt (*IB/A*) with the levorotatory

FIG. 1.

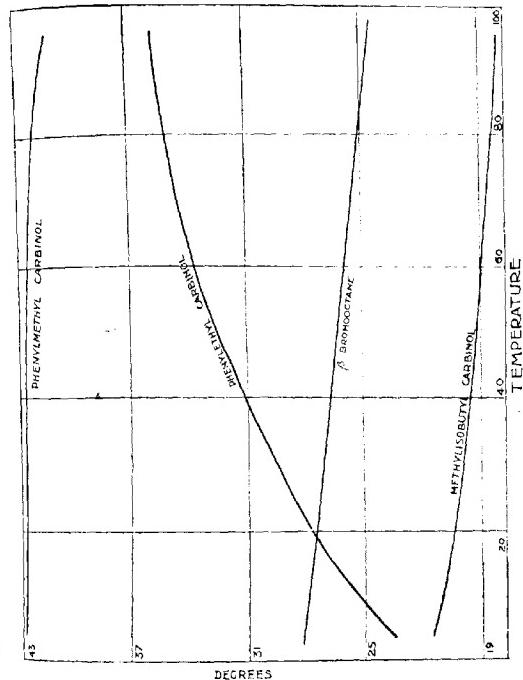
SPECIFIC ROTATORY POWER  
AT DIFFERENT TEMPERATURES

ester. Similar results were obtained with strychnine, whilst cinchonidine gave results of an opposite character, as with this alkaloid the least soluble salts were *IB/A* and *IBdA* in the case of the hydrogen phthalates and succinates respectively. Thus, for example, the following salts were found to be the least soluble component of the mixture of salts formed by neutralising the hydrogen ester with the

base; brucine and strychnine *d*- $\beta$ -heptyl hydrogen phthalate, cinchonidine *t* $\beta$ -heptyl hydrogen phthalate, brucine *d*- $\delta$ -methyl- $\beta$ -amyl hydrogen phthalate, brucine *t*- $\delta$ -methyl- $\beta$ -amyl hydrogen succinate, and cinchonidine *t*-phenylethylcarbinyl hydrogen succinate.

Under the successful conditions employed in the other cases, no

FIG. 2.

SPECIFIC ROTATORY POWER  
AT DIFFERENT TEMPERATURES

resolution was effected with the brucine, strychnine, or cinchonidine salts of the hydrogen phthalates of either phenylmethyl- or phenylethyl-carbinols, or with any salts of the hydrogen esters of tetrachlorophthalic acid.

In the optically pure state, none of the fourteen alcohols has previously been described, except methyl-*n*-heptylcarbinol, the lev-

rotatory isomeride of which was isolated from oil of rue by Power and Lees (*loc. cit.*).

By fermentation methods, Combes and Le Bel (*Bull. Soc. chim.*, 1880, [ii], 33, 106, 147; 1893, [iii], 9, 676) obtained methyl-thyl and methyl-*n*-butyl-carbinols with specific rotatory powers not exceeding  $[\alpha]_D - 0\cdot5^\circ$  and  $[\alpha]_D - 8^\circ$  as against  $[\alpha]_D^{20} + 13\cdot87^\circ$  and  $[\alpha]_D^{20} + 13\cdot70^\circ$  respectively for the pure alcohols, whilst Meth (*Ber.*, 1907, 40, 695) obtained methylethylcarbinol with  $[\alpha]_D$  less than  $1^\circ$  by a method discussed in a former paper by one of us and Littlebury (*loc. cit.*). Marekwald (*Ber.*, 1905, 38, 809) has also obtained phenylmethylcarbinol with  $[\alpha]_D^{20} + 2\cdot7^\circ$  (as against  $[\alpha]_D^{20} + 42\cdot87^\circ$ ) by the action of nitrous acid on *l*-phenylethylamine with  $[\alpha]_D^{20} - 39\cdot51^\circ$ . Hallé (*Compt. rend.*, 1910, 151, 697) has quite recently isolated from cocoa nut oil, feebly dextrorotatory forms of methyl-*n*-heptylcarbinol with  $[\alpha]_D + 2\cdot41^\circ$ , and methyl-*n*-nonylcarbinol with  $[\alpha]_D + 1\cdot40^\circ$ , here rotatory specimens of these having been previously isolated from oil of rue by Power and Lees (*loc. cit.*).

The number of optically active alcohols here described is obviously too small to admit of any discussion of the results in so far as they affect the main object of the investigation. Attention, however, may be drawn to the following points. The rotatory powers of the series of alcohols described do not differ much in general character from some of the series of normal esters described by other investigators, as, for example, the series of the normal esters of diacetylglyceric acid (Frankland, *Trans.*, 1897, 71, 270), where the rotatory power gradually ascends to a maximum. Determinations of the molecular rotatory powers of the hydrogen phthalic esters in chloroform solution gave results\* which run practically parallel with those of the alcohol in the pure state, although in the case of the esters the first member occupies apparently a normal place in the series and has not, as in the case of the alcohols (as also in so many series described by other investigators), an abnormal rotatory power.

At the outset of the investigation it was thought possible that amongst the alcohols of the type  $\text{CH}_3\text{CH}(\text{OH})\text{-R}$ , some simple numerical relation might be found to exist among the numbers expressing the rotatory powers. It will be seen at once, however, that no comparison is feasible, if the influence of temperature be taken into account. Whilst the curves in Fig. 1 relating to the series (methylethyl carbinol excepted) become parallel as the temperature increases, yet at no temperature up to  $100^\circ$  (the limit of the present experiment)\*

\* See table, p. 63.

† The question as to a possible relation or constant existing at or above the boiling points of the alcohols for the molecular rotatory powers is reserved for further discussion when more material is available. The values of the rotatory

can the rotatory powers of the members of the series be compared with those of the alcohols of other types (see Fig. 2), or indeed with that of *methylmethylecarbinol*.

The question of the (as yet unsolved) problem of the effect of association on the rotations of pure liquids (compare Walden, *loc. cit.*) naturally arises in this connexion. Does association account for the great differences in the temperature-coefficients as illustrated in Figs. 1 and 2? Now these alcohols as judged by Ramsay and Shields' capillarity ascension method or by Longinescu's empirical formula\* (*Ann. Sci. Univ. Jassy*, 1903, **2**, 126) are only slightly associated. Thus empirically the association factor for

<i>d</i> -Methylethylecarbinol	is 1.33	<i>d</i> -Methyl- <i>a</i> -nonylcarbinol	is 1.01
<i>d</i> -Methyl- <i>n</i> -propylcarbinol	, 1.21	<i>d</i> -Ethyl- <i>a</i> -hexylcarbinol	, 1.03
<i>d</i> -Methyl- <i>a</i> -butylcarbinol	, 1.15	<i>d</i> -Methylisobutylcarbinol	, 1.14
<i>d</i> -Methyl- <i>n</i> -amylcarbinol	, 1.14	<i>d</i> -Phenylmethylcarbinol	, 1.12
<i>d</i> -Methyl- <i>a</i> -hexylcarbinol	, 1.08	<i>d</i> -Phenylethylcarbinol	, 1.08
<i>d</i> -Methyl- <i>a</i> -heptylcarbinol	, 1.05		

whilst, for example, by the capillarity ascension method *d*-methylethylecarbinol between 19.8° and 36.8° has a mean association factor 1.8, and *d*-methyl-*n*-hexylcarbinol between 15° and 34° has 1.5.† Now the similarity of the temperature-coefficients for the alcohols in the series, despite the decrease in association as the molecular weight increases and the striking differences in the temperature-coefficients of phenylmethyl- and phenylethyl-carbinols, of methyl- and ethyl-*n*-hexylcarbinols, and of methylethylecarbinol and the rest of the series, seems to show that association has a very slight, if any, common influence on the rotation of these pure liquids. Since, however, it is a matter of some difficulty to measure small differences in association, the question of its influence on the rotatory powers of the individual alcohols could not be followed further.

The striking differences observed in the cases just mentioned in the variation of rotatory power with the temperature may be due partly to stereochemical causes, but possibly also to the more profound changes on the rotatory power of a complex,  $R\cdot CII(OH)\cdot CH_2^-$ , caused by hydrogen than by a radicle ( $CH_3^-$ ).

Methylisobutylcarbinol was resolved at an early stage of the investigation to ascertain whether the differences in the rotatory powers of aliphatic alcohols corresponding with small differences in constitution were likely to be large. The exaltation in rotatory power powers of methyl-*a*-butyl- and methyl-*n*-octyl-carbinols commence to rise at about 125°; these being the only two alcohols investigated at the higher temperatures.

\*  $T = \frac{100D}{100D - \sqrt{n}}$ , where  $T = b, p.$  on the absolute scale,  $D = D^0_{4/4}$ , and  $n =$  the mean number of atoms in the molecule.

† It has often been observed that the capillarity ascension method gives higher values for the association factor than those obtained by empirical calculation.

caused by the *isobutyl* as compared with the *n*-butyl group is considerable, and affords additional evidence of powerful influence of constitution on rotatory power.

The halides corresponding with some of the alcohols have been prepared, the molecular rotatory powers being recorded in table III. In every case the conversion of the alcohol into a halide (Cl, Br or I) was accompanied by a change of sign in the rotation. Attempts to reconver these halides into the optically pure alcohols have not as yet proved successful, and the preparation of them with any degree of certainty that racemisation has been avoided is tedious and very costly. This portion of the work has therefore not been extended for the present in case further physical measurements of the alcohols themselves appear desirable as the investigation proceeds. It will be noticed from Fig. 2 that the specific rotation of *d*- $\beta$ -bromo-octane sinks regularly as the temperature increases, the curve being a straight line, and in this respect analogous among the alcohols only with ethyl-*n*-hexylcarbinol, for which, however, the specific rotation rises regularly with the temperature. The association factor for *d*- $\beta$ -bromo-octane, calculated by Longinescu's formula, is 1.07.

The authors are greatly indebted to Dr. T. M. Lowry for the determinations of the refractive indices of the dextrorotatory alcohols as recorded in table IV. Dr. Lowry has also undertaken the determination of the magnetic and optical rotatory dispersion.\* In respect to the optical rotatory dispersion a somewhat striking

TABLE III.  
*Rotatory Powers of the Halides.*

	$[\alpha]_D^{25}$	$[M]_D^{25}$	$[\alpha]_D^{25}$	$[M]_D^{25}$
$\beta$ -Iodo-butane .....	+ 31.98 <sup>2</sup>	- 58.8	—	—
$\beta$ -Iodo-pentane .....	- 37.15	- 57.0	—	—
$\beta$ -Iodo-hexane .....	- 38.35	- 80.9	—	—
$\beta$ -Iodo-octane .....	- 49.56	- 90.4	+ 39.82 <sup>2</sup>	+ 58.5
$\gamma$ -Iodo-nanane .....	- 17.50	- 44.4	+ 17.65	+ 44.8
$\beta$ -Bromo- <i>cis</i> -tane .....	- 27.17	- 51.0	- 27.53	+ 53.1
$\gamma$ -Bromo-nanane .....	- 13.39	- 27.7	+ 12.90	+ 26.7
$\beta$ -Chloro-octane .....	- 20.44	- 30.4	+ 26.40	+ 30.3
$\gamma$ -Chloronanane .....	- 8.03	- 13.0	- 7.71	- 12.5
$\alpha$ -Chloroethylbenzene ...	5.80	- 8.2	—	—
$\alpha$ -Chloropropylbenzene,	3.87	- 6.0	- 3.79	6.0

connexion between this and the anomalous temperature-coefficients already mentioned has been observed. Thus, in a private communication, he states that those active alcohols of which the specific rotatory power varies normally with the temperature (see curves in Fig. 1 for methyl-*n*-propyl- to methyl-*n*-undecyl-carbinol) appear to give a constant value for the ratio  $a_{4670}/a_{5461}$ , which affords the most

\* The results of these determinations will be published separately.

convenient measure of their rotatory dispersion; on the other hand, those alcohols which have a different temperature-coefficient of optical rotatory power (methylethyl-, ethyl-*n*-hexyl-, methylisobutyl-, phenylmethyl-, and phenylethyl-carbinols) also differ in optical rotatory dispersion from the normal series,  $\text{CH}_3\cdot\text{CH}(\text{OH})\cdot\text{R}$  (where  $\text{R} = n\text{-C}_n\text{H}_7$ , to  $n\text{-C}_{11}\text{H}_{23}$ ), of active alcohols referred to above; there is, however, no simple relationship between the sign of the temperature-coefficient and the relative magnitude of the dispersion ratio.

TABLE IV.  
*Refractive Indices of the Dextrorotatory Alcohols.*

Alcohol.	$n_D^{20}$ .	$d_4^{20}$ .	$\frac{n-1}{n+d} \cdot M$ .	Difference for $\text{CH}_2$ .
Methylethylcarbinol .....	1.3954	0.8050	56.2	
Methyl- <i>n</i> -propylcarbinol .....	1.4053	0.8193	44.0	7.4
Methyl- <i>n</i> -butylcarbinol .....	1.4135	0.8150	51.8	7.8
Methyl- <i>n</i> -amylcarbinol .....	1.4209	0.8185	59.6	7.8
Methyl- <i>n</i> -hexylcarbinol .....	1.4256	0.8211	67.4	7.8
Methyl- <i>n</i> -heptylcarbinol .....	1.4299	0.8230	75.2	7.8
Methyl- <i>n</i> -octylcarbinol .....	1.4314	0.8250	83.4	7.9
Methyl- <i>n</i> -nonylcarbinol .....	1.4369	0.8270	91.0	7.9
Methyl- <i>n</i> -decylcarbinol .....	1.4423	0.8315	99.0	8.0
Ethyl- <i>n</i> -hexylcarbinol .....	1.4308	0.8260	75.1	
Phenylmethylcarbinol .....	1.5211	1.9135	63.7	
Phenylisobutylcarbinol .....	1.5260	0.9940	71.1	7.4
Methylisobutylcarbinol .....	1.4103	0.8077	51.8	

It is believed that the present paper shows that synthetical methods may be used to obtain accurate comparative values of the rotatory powers of optically active alcohols. It is hoped that the further investigation of several other series of alcohols and also of acids of similar constitution may give values which will be capable of easier interpretation in a quantitative manner than the results of those investigators who have preceeded the present authors in this field.

#### EXPERIMENTAL.

##### *The Racemic Alcohols.*

Of the fourteen racemic secondary alcohols which have been investigated, thirteen\* have been prepared either by the interaction of an aldehyde and a Grignard reagent, or by the reduction of the corresponding ketone in aqueous alcoholic solution with sodium.

The reactions between acetaldehyde and magnesium ethyl bromide, magnesium propyl bromide (or chloride), and magnesium isobutyl bromide respectively; between *n*-heptaldehyde and magnesium ethyl bromide; between *n*-octaldehyde and magnesium methyl iodide, and

\* Methyl-*n*-hexylcarbinol is obtained commercially by the distillation of a castor oil soap with sodium hydroxide.

between benzaldehyde and magnesium methyl and ethyl iodides all proceed smoothly, and were carried out in the usual manner, the cheaper reagent being used in slight excess. In this way 50 to 70 per cent. yields were obtained of crude methylethylcarbinol (b. p. 92–99°),\* methyl-n-propylcarbinol (b. p. 118–122°),† methylisobutylcarbinol (b. p. 125–132°),† ethyl-n-hexylcarbinol (b. p. 118–121°/65 mm.), methyl-n-heptylcarbinol (b. p. 91°/12 mm.), phenylmethylcarbinol (b. p. 100°/18 mm.),‡ and phenylethylcarbinol (b. p. 105–108°/10 mm.).‡

The reaction between magnesium *n*-butyl iodide and acetaldehyde gave only about 10 per cent. of the calculated yield of methyl-*n*-butylcarbinol (b. p. 136°), whilst methyl-*n*-heptylcarbinol and methyl-*n*-octylcarbinol form a very small proportion of the products formed by the reactions between acetaldehyde and magnesium *n*-heptyl and *n*-octyl iodides.

The *n*-octaldehyde used was prepared from *n*-octyl alcohol by Sabatier's excellent method for the conversion of primary alcohols into the corresponding aldehydes. The alcohol was heated in a flask, which was surrounded by a metal-bath kept at 200°. A rapid current of pure hydrogen passing through this flask carried the alcohol to a glass tube of which 50 cm. were packed with pumice stone covered with finely divided copper, and which was heated to 300–315°. The aldehyde was washed out of the condensed products by a solution of sodium hydrogen sulphite, and the process repeated four times with the unconverted alcohol. The sodium hydrogen sulphite compound of *n*-octaldehyde was crystallised from aqueous alcohol, and obtained in numerous leaflets, which did not melt below 270°. Decomposition of this compound with a strong solution of sodium carbonate, distillation of the product in a current of steam, and subsequent rectification gave a 50 per cent. yield (calculated from the alcohol used) of *n*-octaldehyde (b. p. 77°/23 mm.). No by-products were observed in this preparation, the loss being due very largely to inefficient condensation of the products carried over by the hydrogen.

The ketones required,  $\text{CH}_3\text{CO}\cdot\text{R}$ , were prepared by passing the various acids,  $\text{R}\cdot\text{CO}_2\text{H}$ , mixed with five to seven times their weight of glacial acetic acid, over thorium oxide heated to 400° (Senderens, *Compt. rend.*, 1909, **149**, 995 *et seq.*). The thoria was mixed with glass wool and loosely packed into a tube of Jena glass heated for 50 cm. of its length. The normal acids used were hexoic, nonoic,

\* Methylethylcarbinol requires careful and repeated fractionation to separate it from ether.

† Both of these crude alcohols contained paracetabdehyde.

‡ Each of these alcohols had a peculiar characteristic and pungent odour, which was not removed by repeated distillation, but was not present in the optically active isomerides.

undecenoic, and lauric acid. The solutions of these in acetic acid were passed through the slightly inclined tube from a dropping funnel at an hourly rate of about 50 c.c. In each case the products were practically neutral, and no charring took place in the heated tube. Fractional distillation of the products gave from 70 to 90 per cent. yields (calculated from the weight taken of the acids named) of the ketones of the general formula  $\text{CH}_3\text{CO}\cdot\text{R}$ , and from 30 to 10 per cent. yields of the ketones with the formula  $\text{R}\cdot\text{CO}\cdot\text{R}$ . The methyl *n*-amyl ketone prepared in this manner was identical with a sample of the same compound purchased from Schuchardt, which had been prepared by the distillation of a mixture of barium hexoate and acetate. Some properties of the ketones prepared are set out in table V.

TABLE V.

Ketone.	Melting point.	Boiling point.	Melting point of semicarbazone.*
Methyl <i>n</i> -amyl ketone .....	—	150°	123°0
Methyl <i>n</i> -octyl    "	—	210	121°5
Methyl <i>n</i> -decyl    "	20°	144°/11 mm.	122°-123
Methyl <i>n</i> -undecyl    "	29	160°/16 mm.	126°0
Diamyl    "	—	223°	—
Diocetyl    "	53	—	—
†Didecyl    "	64	—	—
Diundecyl    "	70-71	—	—

\* All obtained from aqueous alcohol in the form of prismatic needles.

† The oxime of this ketone crystallises from aqueous needles in hair-like needles, which melt at 27·5°, and readily regenerates the ketone when boiled with dilute hydrochloric acid.

It will be seen that the semicarbazones are of little value for the characterisation of the ketones,  $\text{CH}_3\text{CO}\cdot\text{R}$ , for these all melt at about 123°, whilst the ketones,  $\text{R}\cdot\text{CO}\cdot\text{R}$  (where R contains more than five carbon atoms), do not form semicarbazones by the ordinary methods for the preparation of these compounds.

The nonoic and undecenoic acids used in the preparation of the above-mentioned ketones were obtained in almost quantitative yields\* by Darzens' method (*Compt. rend.*, 1907, **144**, 329), in which the ethyl esters of  $\Delta^1$ -nonylenic acid † and commercial undecenoic acid were reduced by hydrogen in the presence of finely divided nickel heated to 180°.

\* Thus, for example, in one set of experiments 300 grams of undecenoic acid were esterified and reduced. After hydrolysis of the resulting saturated ester and distillation of the acid, 260 grams of undecenoic acid (m. p. 28°) were obtained. From this was prepared 174 grams of methyl *n*-decyl ketone along with a quantity of didecyl ketone, 43 grams of the acid being recovered; 133 grams of methyl-*n*-decyl-carbinol were obtained by the reduction of this ketone.

†  $\Delta^1$ -Nonylenic acid was prepared by the excellent method of Hardig and Neumann (*Trans.*, 1910, **97**, 299).

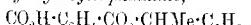
The ketones of the general formula  $\text{CH}_3\cdot\text{CO}\cdot\text{R}$ , as described above, and also methyl *n*-butyl ketone and methyl *n*-nonyl ketone (purchased from Kahlbaum) were reduced in alcoholic solution by means of sodium, the procedure of Thoms and Mannich (*Ber.*, 1903, **36**, 2544) adopted for their reduction of methyl *n*-nonyl ketone being followed. The alcohols\* thus obtained were (the yields varying from 70–80 per cent.): methyl-*n*-butylcarbinol (b. p. 136°), methyl-*n*-amylecarbinol (b. p. 158–160°), methyl-*n*-octylcarbinol (b. p. 210–211°), methyl-*n*-nonylcarbinol (b. p. 119°/12 mm.), methyl-*n*-decylcarbinol (m. p. about 5°, b. p. 140°/15 mm.), and methyl-*n*-undecylcarbinol (b. p. 151°/11 mm.).

#### *The Racemic Hydrogen Phthalic Esters.*

The hydrogen phthalic esters were prepared by heating the alcohols with phthalic anhydride (equal mols.) for about ten hours at 115° in an oil-bath, except in the case of methylethyl- and methyl-*n*-propylcarbinols, which were heated on a water-bath. The products, which generally contained some phthalic acid and unaltered anhydride, were poured when cold into a solution of sodium carbonate. After keeping for some hours to allow of the hydrolysis of any anhydride, the alkaline solutions were extracted three times with ether to remove unesterified alcohols and neutral phthalic esters, both of which dissolve to a considerable extent in aqueous solutions of the sodium alkyl phthalates.\* The acid esters were then precipitated by hydrochloric acid, either as oils or solids of low melting point, and were extracted with chloroform. Phthalic acid, being insoluble in dry chloroform, is thus readily removed, whilst the dried extracts after complete removal of the chloroform, at first on a water-bath, and finally under diminished pressure, consisted of the hydrogen phthalates in the form of opaque, crystalline masses. These acid esters are very soluble in all the common organic media, but some of them crystallise readily from light petroleum. The melting points of the racemic hydrogen phthalates are recorded in table IX, p. 63, along with those of the corresponding active compounds, whilst the composition and purity of each were checked by titration in alcoholic solution with sodium hydroxide.

The following compounds were also obtained :

*Phenylmethylcarbinyl hydrogen phthalate,*

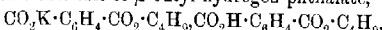


which crystallises in opaque leaflets from either glacial acetic acid or benzene, and melts at 108°.

\* All these alcohols were comparatively much purer than those obtained by the Grignard reactions.

† Such solutions cannot be warmed to 70° or above without undergoing some decomposition.

An acid potassium salt of  $\beta$ -butyl hydrogen phthalate,



which crystallises from acetone in very slender needles, melts at  $160-168^\circ$ , and is decomposed by warm water.

Found, K = 8.07.  $\text{C}_{24}\text{H}_{27}\text{O}_8\text{K}$  requires K = 8.09 per cent.

#### *The Racemic Hydrogen Succinates.*

Several acid esters of succinic acid were prepared by a method similar to that employed for the corresponding phthalates. They are, however, best extracted by ether instead of chloroform, traces of succinic acid being readily removed from the ethereal solutions by washing with water. The following carbinols gave hydrogen succinates in the form of viscous oils which did not solidify when kept at  $-10^\circ$ : methylethyl-, methyl-n-propyl-, methyl-n-butyl-, methyl-n-nonyl-, methylisobutyl-, and phenylethyl-carbinols, whilst that of phenyl-methylcarbinol crystallises from light petroleum in beautiful nacreous leaflets, and melts at  $60-61^\circ$ .

#### *Brucine Salts of the Acid Esters.*

The method adopted in each case for the preparation of the pure brucine salt of the dextrorotatory acid ester was: A solution of pure\* racemic acid ester in acetone is boiled with the calculated amount (equal mols.) of brucine,<sup>†</sup> which is added in small portions at a time until the alkaloid is completely dissolved. The solution, having been filtered (if necessary) while warm, is then concentrated, and set aside in the ice-chest for some hours. The crop of crystals is collected and recrystallised several times under the same conditions. The first mother liquor when acidified yields a levorotatory acid ester, and is used for the preparation of the pure levorotatory alcohol, whilst that from the first recrystallisation yields an acid ester, which is usually slightly dextrorotatory, and can be conveniently used for the preparation of the strychnine salt of the pure dextrorotatory acid ester. The melting points and rotation of the brucine salts become constant after three to ten crystallisations, whilst in most cases the solubility in warm acetone decreases to a considerable extent as the salt becomes pure. The actual solubility of the pure salts of the phthalates varies considerably and most irregularly even in the homologous series described (see table VI); thus, for example, in the case of the member of the series corresponding with octane, 100 grams of the pure brucine salt would require about 10 litres of hot acetone to dissolve it,

\* The success of the resolution largely depends on the purity of the acid ester.

† All the alkaloids mentioned in this paper were the purest commercial specimens supplied by Merck, and were recovered unchanged in rotation.

whilst the same quantity of the salt of that corresponding with nonape would require less than half a litre. The composition of the brucine salts, as well as of the other alkaloidal salts described in this paper, was determined by an estimation of the nitrogen content. In every case, as was to be expected, the salt contained one molecule of each component. The brucine salts of the acid esters of succinic acid are, as a rule, much more soluble in acetone than the salts of the corresponding phthalates. The following salts were also prepared : *Dibrucine phthalate*,  $C_{34}H_{55}O_{12}N_4$ , which crystallises from warm alcohol in glistening lamella, which melt and decompose at  $113^\circ$ , and are very slightly soluble in cold alcohol or chloroform. *Brucine hydrogen phthalate*,  $C_{31}H_{32}O_8N_2$ , which crystallises from alcohol in clusters of prismatic needles, melts at  $216^\circ$ , and when dissolved in chloroform has  $[\alpha]_D +13.52^\circ$ . *Brucine hydrogen succinate*,  $C_{27}H_{32}O_8N_2$ , crystallises from aqueous alcohol in needles, melts at  $217-219^\circ$ , and in absolute ethyl alcohol has  $[\alpha]_D -17.70^\circ$ .

TABLE VI.

*Brucine Salts.*

Brucine salt of the <i>hydrogen phthalate</i> of	Melting point	Rotatory power* in ethyl alcohol.	
		Specific.	Molecular.
<i>d</i> -Methylethylcarbinol	154-155°	-2.93°	-18.1°
<i>d</i> -Methyl- <i>n</i> -propylcarbinol	154-155	-3.91	24.6
<i>d</i> -Methyl- <i>n</i> -butylcarbinol	144-145	4.04	26.0
<i>d</i> -Methyl- <i>n</i> -amylcarbinol	137-138	4.42	29.1
<i>d</i> -Methyl- <i>n</i> -hexylcarbinol	151	5.44	36.6
<i>d</i> -Methyl- <i>n</i> -heptylcarbinol	140-142	4.97	34.1
<i>d</i> -Methyl- <i>n</i> -octylcarbinol	136-138	6.01	42.1
<i>d</i> -Methyl- <i>n</i> -nonylcarbinol	113-116	5.22	37.2
<i>d</i> -Methyl- <i>n</i> -decylcarbinol	123-124	6.06	44.1
<i>d</i> -Methyl- <i>n</i> -undecylcarbinol	120-122	5.69	42.2
<i>d</i> -Methylisobutylcarbinol	167-168	4.19	26.9
<i>d</i> -Ethyl- <i>n</i> -hexylcarbinol	108-110	11.41	78.5
<i>hydrogen succinate</i>			
<i>d</i> -Phenylmethylcarbinol	110.5	+15.33	+94.4
<i>d</i> -Phenylethylcarbinol	103-105	16.28	100.2
<i>d</i> -Methylisobutylcarbinol	95	22.41	-139.6

\* In all cases mentioned in this paper where the rotatory power of a compound has been observed in solution, the solution was prepared by making up 1 gram of the compound to 20 c.c. with the solvent.

*Cinchonidine and Strychnine Salts of the Acid Esters.*

The cinchonidine salts of the acid esters were prepared, as a rule, in the same way as the brucine salts, but when dissolved in hot acetone they often decompose and deposit the alkaloid. It was found preferable in some cases to adopt the following method, which was employed for the preparation of the strychnine salts : Equimolecular proportions

of the alkaloid and the acid ester are dissolved in chloroform; the chloroform is then distilled off, and whilst the salt is still in the pasty condition, it is dissolved by the addition of the requisite amount of boiling acetone. For each recrystallisation the salt is dissolved in chloroform, and a like procedure followed.

Most of the cinchonidine salts are very soluble in acetone, and do not crystallise at all readily from aqueous acetone. The strychnine salts of the optically pure acid esters are only very slightly soluble in cold acetone, and are always partly decomposed when boiled with acetone. The strychnine salts described in table VIII were all prepared from samples of acid esters possessing a slight positive rotation. Strychnine salts of the *d*-hydrogen phthalates were unaltered in rotation by recrystallisation in the manner described, whilst the rotation of the strychnine salt of a partially active hydrogen phthalate of phenylmethylcarbinol was not affected by crystallisation.

TABLE VII.  
*Cinchonidine Salts.*

Cinchonidine salt of the hydrogen phthalate of	Melting point.	Rotation in ethyl alcohol.	
		Specific.	Molecular.
<i>t</i> -Methyl- <i>n</i> -amylcarbinol	108-109°	-70.36°	-392.6°
<i>t</i> -Methyl- <i>n</i> -hexylcarbinol	112-116	68.92	389.0
<i>t</i> -Ethyl- <i>n</i> -hexylcarbinol	115-118	60.47	354.3
<i>hydrogen succinate of</i>			
<i>d</i> -Methyl- <i>n</i> -butylcarbinol	89-90	76.73	359.6
<i>d</i> -Methylisobutylcarbinol	100-102	76.54	379.6
<i>t</i> -Phenylisobutylcarbinol	161-162	118.16	628.2

TABLE VIII.  
*Strychnine Salts.*

Strychnine salt of the hydrogen phthalate of	Melting point.	Rotation in chloroform.	
		Specific.	Molecular.
<i>d</i> -Methylethylecarbinol	149-152°	-20.61°	-27.8°
<i>d</i> -Methyl- <i>n</i> -propylcarbinol	179-181	-18.56	30.7
<i>d</i> -Methyl- <i>n</i> -amylcarbinol	203-204	18.89	51.7
<i>d</i> -Methyl- <i>n</i> -hexylcarbinol	180	18.74	32.7
<i>d</i> -Methyl- <i>n</i> -heptylcarbinol	142-143	-19.47	32.2
<i>d</i> -Methyl- <i>n</i> -octylcarbinol	136-137	-18.37	34.8
<i>d</i> -Methyl- <i>n</i> -nonylcarbinol	144-145	17.11	38.2
<i>d</i> -Methyl- <i>n</i> -undecylcarbinol	142-143	-18.69	36.6

#### *Optically Active Acid Esters of the Alcohols.\**

The optically active acid esters were readily obtained from the brucine and cinchonidine salts when alcoholic solutions of these were

\* Attempts were made to resolve the hydrogen tetrachlorophthalic esters of methyl-*n*-methyl-, methyl-*n*-butyl-, methyl-*n*-propyl-, and methyl-*n*-butyl-carbinols by fractional crystallisation of the brucine and cinchonidine salts, but in no case was any resolution effected under the conditions tried.

poured into dilute hydrochloric acid. Although the oily esters, which were at once precipitated, in many cases solidified to crystalline masses, it was generally found necessary to dissolve them in ether, so that by repeated washing with very dilute hydrochloric acid the hydrochloride of the alkaloid could be completely removed. The strychnine salts were decomposed in a somewhat different manner. Alcoholic solutions of these were poured into dilute ammonia, and, after the strychnine had been removed by filtration, the acid esters were obtained on the addition of hydrochloric acid.

The acid phthalic esters (see table IX) were all obtained as crystalline masses after removal of the solvent, and in some cases are readily recrystallised from light petroleum, but, like the acid succinic acids and all the corresponding racemic compounds, they are very soluble in the common organic media. The optically active acid succinic esters were only isolated in three cases, being usually hydrolysed at once. They are all oils, which decompose when distilled, so that the observed rotatory powers may be misleading, as the solvent (ether) may not have been completely removed. The hydrogen succinate of *d*-methylisobutylcarbinol had  $[\alpha]_D + 14.52^\circ$  in chloroform, and the corresponding laevo-compound,  $[\alpha]_D - 14.37^\circ$ ; *d*- $\beta$ -hexyl hydrogen succinate had  $[\alpha]_D + 6.19^\circ$  in chloroform, whilst the hydrogen succinate of phenylethylcarbinol had  $\alpha - 20.06^\circ$  in a 25-mm. tube.

#### *The Optically Active Alcohols.*

The alcohols, except in the case of methylethyl- and methyl-*n*-undecyl-carbinols, were obtained by the following method: The acid ester is dissolved in a hot concentrated aqueous solution of potassium hydroxides ( $2\frac{1}{2}$  mols.), and the alcohol formed by the hydrolysis is distilled over in a current of steam. It is then extracted from the distillate by ether, and the ethereal solution is dried by long keeping over freshly ignited potassium carbonate.

The optically active alcohols obtained were comparatively stable in the presence of alkali hydroxides. Although as a matter of precaution they were removed from the prolonged action of potassium hydroxide as rapidly as possible by a current of steam during the hydrolysis, yet in two or three cases (notably those of methyl-*n*-hexyl- and methyl-*n*-undecyl-carbinols) by actual experiment it was found that the rotation was unaltered by continued boiling under a reflux condenser with aqueous alkalis. The alcohols were obtained as colourless, strongly refracting liquids or low melting solids. They have faint characteristic odours, in all cases these being far less than those of the optically inactive isomerides. There seems to be in some cases, for

TABLE IX.  
*The Hydrogen Phthalic Esters.*

Hydrogen phthalate of	Melting point of Racemic.	Activ. [α] <sub>D</sub>	Phthalic form.		Rotations in ethyl alcohol. [M] <sub>D</sub>	Origin of ester. <sup>f</sup>
			[α] <sub>D</sub>	[M] <sub>D</sub>		
Methyl- <i>o</i> -phenylcarbinol	56—57*	+36—47*	+33.54	+74.57	+38.97*	B
Methyl- <i>o</i> -propylcarbinol	56—57*	—	+33.51	+74.4	—	S
Methyl- <i>o</i> -butylcarbinol	56—61	+34	+36.94	+87.9	—	S
Methyl- <i>o</i> -isobutylcarbinol	56—61	+29	+43.39	+108.5	+47.02	B
Methyl- <i>o</i> -methylcarbinol	57—58	76.5	+43.89	+115.9	+48.64	B
Methyl- <i>o</i> -n-butylcarbinol <sup>g</sup>	57—58	—	+43.94	+116.0	+128.4	S
Methyl- <i>o</i> -n-pentylcarbinol <sup>g</sup>	—	—	+43.81	+116.7	+48.52	C
Methyl- <i>o</i> -hexylcarbinol <sup>g</sup>	55	75	+42.94	+119.3	+48.06	B
Methyl- <i>o</i> -heptylcarbinol <sup>g</sup>	55	—	+43.27	+120.3	+48.25	C
Methyl- <i>o</i> -octylcarbinol <sup>g</sup>	58—59	—	+41.17	+120.1	+46.06	B
Methyl- <i>o</i> -heptylacetinol <sup>g</sup>	42—44	—	+41.04	+118.9	—	S
Methyl- <i>o</i> -heptylacetinol <sup>g</sup>	48—50	+38—39	+39.01	+119.3	+45.19	B
Methyl- <i>o</i> -heptylacetinol <sup>g</sup>	48—50	+31—32	+39.11	+119.7	—	S
Methyl- <i>o</i> -heptylacetinol <sup>g</sup>	48—50	—	+37.34	+119.5	—	B
Methyl- <i>o</i> -decylcarbinol	50—53	—	+37.19	+118.8	+44.29	S
Methyl- <i>o</i> -decylcarbinol	58—59	+28	+35.59	+121.9	+43.41	B
Methyl- <i>o</i> -undecylcarbinol	—	+26	+35.54	+124.0	+44.13	B
Methyl- <i>o</i> -undecylcarbinol	47—49	—	+35.13	+122.3	—	S
Methyl- <i>o</i> -undecylcarbinol	47—49	51—55	+13.78	+10.9	+19.40	B
Methyl- <i>o</i> -undecylcarbinol	47—49	—	+13.62	+19.6	+27.9	C
Methyl- <i>o</i> -undecylcarbinol	47—49	—	—	—	+19.45	—
Methyl- <i>o</i> -undecylcarbinol	47—49	—	—	—	+28.0	—

\* Denotes a melting point determined of the crystalline mass dried on a borosilicate tile without recrystallisation.

<sup>†</sup> B denotes from brucine salt; S from strychnine salt, and C from curchonidine salt.

example, phenylethylcarbinol, a slight difference in the aroma of the dextrorotatory and laevorotatory forms.

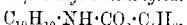
Specimens of some of the alcohols of each type described were found to be unaltered in rotatory power after exposure to light for many months whilst stored in common glass bottles. Several of them were reconverted into the hydrogen phthalic esters, these being readily obtained without recrystallisation with the maximum rotation observed, showing that at least these alcohols will not undergo racemisation when removed from natural products by the "phthalic anhydride" method (compare Haller, *Compt. rend.*, 1910, **151**, 697). At least 30 c.c. of each of the active alcohols mentioned below have been obtained and the preparations repeated. The densities have been determined in a pyknometer holding 3·5 c.c., and the rotations in jacketed tubes of 50 and 100 mm. long.

*Methylethylcarbinol*.—Since this alcohol is very difficult to separate from ether, it was "salted out" of the distillate obtained from the hydrolysis of the hydrogen phthalic ester by means of potassium carbonate. Specimens of the dextrorotatory alcohol obtained from the brucino and strychnine salts of this acid ester agreed in rotatory power, this being unaltered by keeping over freshly-ignited barium oxide.

The dextrorotatory alcohol boiled at 99°/760 mm., had  $d_4^{20}$  0·8106,  $\bar{\tau}$  0·8025,  $[\alpha]_D^{20}$  0·7717, and  $\bar{\tau}^2$  0·7566; and  $[\alpha]_D + 14\cdot83^\circ$  at  $4\cdot5^\circ$ ,  $+11\cdot0^\circ$  at  $17\cdot8^\circ$ ,  $+13\cdot52^\circ$  at  $27^\circ$ ,  $+13\cdot08^\circ$  at  $36\cdot5^\circ$ ,  $+12\cdot57^\circ$  at  $48\cdot7^\circ$ ,  $+12\cdot15^\circ$  at  $58^\circ$ ,  $+11\cdot77^\circ$  at  $72^\circ$ , and  $+11\cdot83^\circ$  at  $91\cdot7^\circ$ .

The alkaloidal salts of the *l*- $\beta$ -butyl hydrogen phthalate and of the corresponding succinates crystallise badly, and are decomposed when warmed with acetone.

Several attempts have been made by one of us and W. O. Littlebury to resolve this alcohol by the "menthylcarbimide" method (see *Trans.*, 1906, **89**, 465, 1254). *Dl*- $\beta$ -Butyl *l*-menthylcarbamate,



was readily obtained by warming equimolecular quantities of the carbinol and *l*-menthylcarbamide. It crystallises in large prismatic tablets, which melt at 54°, and have  $M_D - 162\cdot4$  in chloroform.

When recrystallised several times from aqueous ethyl alcohol, the melting point rose to 71°, and the molecular rotatory power fell to  $-152\cdot4^\circ$ . The resolution, however, was not complete, as *d*- $\beta$ -butyl *l*-menthylcarbamate, prepared from the dextrorotatory alcohol described above, melted at 72°, and had  $[\alpha]_D - 55\cdot78^\circ$  and  $M_D - 142\cdot2^\circ$  in chloroform. Experiments in this direction were not completed, as it was found impossible to hydrolyse the carbamate except by means of alcoholic potassium hydroxide, and then the separation of the carbinol from the ethyl (or methyl) alcohol used required too much material.

*1-β-Iodobutane.*—Several comparative experiments were carried out to determine the conditions for displacing the hydroxyl group of the arabinol by iodine without racemisation of the compounds. The product of highest levorotatory power was obtained when the dextro-rotatory alcohol was saturated at 0° with hydrogen iodide (free from iodine) and warmed in a sealed tube for thirty minutes at a temperature not exceeding 60°. The levorotatory iodo-compound thus prepared boiled at 118°, had  $d_4^{25} 1.5970$ , and  $[\alpha]_D^{25} -31.98^{\circ}$ . Attempts to convert this iodide into optically active methylethylcarbinol (*sec.-butylcarbinol*) by successive treatment with magnesium in ethereal solution and formaldehyde (trioxymethylene) gave negative results; under the conditions tried, the products were always optically inactive, racemisation probably taking place during the formation of the Grignard reagent.

*d-Methyl-n-propylcarbinol.*—This alcohol, prepared either from the racine or the strychnine salt of the dextrorotatory hydrogen phthalic ester, boiled at 118.5—119.5°. Determinations of the density gave  $d_4^{25} 0.8169$ ,  $d_4^{28} 0.8058$ ,  $d_4^{29} 0.7967$ ,  $d_4^{33} 0.7871$ ,  $d_4^{60} 0.7751$ ; and of the specific rotatory power:  $[\alpha]_D^{25} +14.38^{\circ}$ ,  $+13.86^{\circ}$  at 19°,  $+13.44^{\circ}$  at 75°,  $+13.14^{\circ}$  at 38°,  $+12.91^{\circ}$  at 49°,  $+12.79^{\circ}$  at 58.5°,  $+12.55^{\circ}$  at 3°, and  $+12.56^{\circ}$  at 90.5°.

*1-β-Iodopentane.*—This compound was prepared as follows: The extracrotatory alcohol was saturated with pure hydrogen iodide at 0°, and heated at 100° in a sealed tube for thirty minutes. After purification in the usual manner, the iodide boiled at 143°, had  $d_4^{25} 1.5067$ , and  $[\alpha]_D^{25} -37.15^{\circ}$ .

*d-Methyl-n-butylcarbinol*, of identical rotatory power, was obtained from the brucine salt of the dextrorotatory hydrogen phthalic ester and from the cinchonidine salt of the dextrorotatory hydrogen succinic ester. It boiled at 137—138°, had  $d_4^{25} 0.8179$ ,  $d_4^{27} 0.8021$ ,  $d_4^{28} 0.7903$ ,  $d_4^{29} 0.7726$ , and  $d_4^{33} 0.7134$ , and  $[\alpha]_D^{25} +12.08^{\circ}$ ,  $+11.60^{\circ}$  at 19°,  $+11.45^{\circ}$  at 26.8°,  $+11.27^{\circ}$  at 35.7°,  $+11.05^{\circ}$  at 48°,  $+10.87^{\circ}$  at 59°,  $+10.77^{\circ}$  at 72°,  $+10.77^{\circ}$  at 93°, and  $+11.28^{\circ}$  at 133°.

*1-β-Iodoxhexane* was prepared in a similar manner to the corresponding pentane derivative. It had  $d_4^{25} 1.4354$ , and  $[\alpha]_D^{25} -38.35^{\circ}$ .

*d-Methyl-n-amylcarbinol.*—This alcohol boiled at 73.5°/20 mm., had  $d_4^{25} 0.8190$ ,  $d_4^{27} 0.8050$ ,  $d_4^{28} 0.7920$ ,  $d_4^{29} 0.7815$ , and  $[\alpha]_D^{25} +10.21^{\circ}$ ,  $+10.14^{\circ}$  at 31°,  $+9.95^{\circ}$  at 46°, and  $+9.75^{\circ}$  at 69.3°.

*1-Methyl-n.amylcarbinol* had very similar constants to the dextro-rotatory alcohol. It boiled at 74.5°/23 mm., had  $d_4^{25} 0.8184$ , and  $[\alpha]_D^{25} -10.52^{\circ}$ ,  $-10.48^{\circ}$  at 17°, and  $-9.58^{\circ}$  at 91°.

*d- and 1-Methyl-n-hexylcarbinols.*—These alcohols (Pickard and Kenyon; *loc. cit.*) have been prepared in larger quantities than any of the other alcohols here described. The following additional

constants have been determined for the dextrorotatory compound:  $d_4^{20}$  0.8170,  $d_4^{25}$  0.8095,  $d_4^{40}$  0.8019, and  $[\alpha]_D +10.00^\circ$  at  $9^\circ$ ,  $+9.51^\circ$  at  $25.5^\circ$ ,  $+9.40^\circ$  at  $35.5^\circ$ ,  $+9.19^\circ$  at  $48^\circ$ , and  $+8.98^\circ$  at  $91.5^\circ$ .

*Dl-Methyl-n-hexylcarbinol.*—Several investigators have observed that ordinary commercial methylhexylcarbinol (*sec*-octyl alcohol) possesses a slight rotatory power. Samples supplied by Kahlbaum had  $a^{25} -0.15^\circ$  in a 2-dcm. tube. This alcohol was converted into the hydrogen phthalic ester, and recrystallised twice from glacial acetic acid and once from light petroleum. The alcohol recovered from this purified ester possessed approximately the same rotatory power. It was therefore assumed that the commercial alcohol contained a small amount of the *l*-alcohol. To it was then added the calculated amount of the *d*-alcohol, so that an inactive product was obtained. This was treated with phthalic anhydride, and the ester purified as before. The alcohol prepared by the hydrolysis of this thrice-recrystallised ester was found to be completely inactive. The experiments described below, in which an inactive methylhexylcarbinol was used, were carried out with a product prepared in this way.

#### *Esters of Methyl-n-hexylcarbinol.*

*Dl-β-Octylacetate*,  $\text{CH}_3\text{CO}_2\text{CHMe}\cdot\text{C}_6\text{H}_5$ .—This was obtained as a pleasant-smelling, mobile liquid, boiling at  $86-88^\circ/22$  mm. It had  $d_4^{20}$  0.8569, and  $[\alpha]_D^{25} +7.65^\circ$ , whilst when hydrolysed with potassium hydroxide it gave the optically pure *d*-alcohol.

*Dl-β-Octyl β-phenylpropionate*,  $\text{C}_6\text{H}_5\text{CH}_2\text{CO}_2\text{CHMe}\cdot\text{C}_6\text{H}_{13}$ .—The acid was converted into the chloride by heating on the water-bath with the calculated amount of thionyl chloride. The product was then warmed with the *d*-alcohol until hydrogen chloride ceased to be evolved. The oily ester was then purified in the usual manner, and it was found that redistillation did not alter its rotatory power:

0.1176 gave 0.3354  $\text{CO}_2$  and 0.1036  $\text{H}_2\text{O}$ . C = 77.78; H = 9.80.

$\text{C}_{17}\text{H}_{26}\text{O}_2$  requires C = 77.86; H = 9.92 per cent.

The ester is a transparent and odourless liquid of somewhat viscous character, which boils at  $192-196^\circ/27$  mm., and has  $d_4^{20}$  0.9483. The rotation observed in a 1-dcm. tube gave  $\alpha_D +11.56^\circ$ , whence  $[\alpha]_D^{25} +12.19^\circ$ . A second preparation, made by the method of saturating a solution of the acid in the *d*-alcohol with hydrogen chloride, had  $[\alpha]_D^{25} +12.26^\circ$ .

The corresponding *laevo*-compound was prepared in a similar manner by the first of the methods indicated above. It boils at  $200-202^\circ/32$  mm., and has  $d_4^{20}$  0.9476. In a 1-dcm. tube it gave  $\alpha_D -11.85^\circ$ , whence  $[\alpha]_D^{25} -12.51^\circ$ . From each of these two esters there were

recovered, by hydrolysis, alcohols with  $[\alpha]_D^{25} \pm 9.9^\circ$ . The corresponding inactive ester boils at  $190\text{--}192^\circ/27$  mm., and has  $d_4^{17} 0.9815$ .

*Esters of Cinnamic Acid.*—These were prepared by passing hydrogen chloride for forty-five minutes through a mixture of equivalent proportions of the alcohols and cinnamic acid, which was kept at  $110^\circ$ . The esters were purified in the usual manner, and were obtained as clear, colourless liquids without odour.

The *d*- $\beta$ -octyl cinnamate thus prepared boiled at  $218^\circ/28$  mm., had  $d_4^{\circ} 0.9694$ , and in a 50-mm. tube  $a^{17} + 19.48^\circ$ , whence  $[\alpha]_D^{25} + 40.19^\circ$ . The alcohol recovered from this ester had  $[\alpha]_D^{25} + 9.68^\circ$ . The ester, which was quite free from chlorine, when repeatedly treated with aluminium amalgam in moist ethereal solution was quantitatively converted into the corresponding ester of  $\beta$ -phenylpropionic acid, which had  $[\alpha]_D^{25} + 12.36^\circ$ .

The corresponding *laevo*-ester boiled at  $211^\circ/23$  mm., had  $d_4^{\circ} + 0.9692$ , and  $[\alpha]_D^{25} - 39.78^\circ$ , whilst the *dL*-ester boiled at  $213^\circ/28$  mm., and had  $d_4^{\circ} 0.9715$ :

0.1261 gave 0.3620 CO<sub>2</sub> and 0.1065 H<sub>2</sub>O. C = 78.51; H = 9.38.  
 $C_{17}H_{24}O_2$  requires C = 78.46; H = 9.23 per cent.

*Esters of Phenylpropioic Acid.*—The esters of phenylpropioic acid were prepared in the same manner as those of cinnamic acid. They were obtained free from chlorine, and when hydrolysed gave the optically pure alcohols. They are colourless, highly refractive liquids, which possess faint odours. The *d*-ester boiled at  $206\text{--}208^\circ/20$  mm., had  $d_4^{\circ} 0.9823$ , and in a 50-mm. tube gave  $a^{17} + 24.95^\circ$ , whence  $[\alpha]_D^{25} + 50.80^\circ$ . Repeated treatment with aluminium amalgam in moist ethereal solution converted the unsaturated ester into the corresponding derivative of  $\beta$ -phenylpropionic acid, which had  $[\alpha]_D^{25} + 12.06^\circ$ . The *l*-ester boiled at  $209^\circ/27$  mm., had  $d_4^{\circ} 0.9719$ , and gave  $a^{17} - 12.33^\circ$  in a 25-mm. tube, whence  $[\alpha]_D^{25} - 50.75^\circ$ . The *dL*-ester boiled at  $228\text{--}231^\circ/48$  mm., and had  $d_4^{\circ} 0.9757$ .

*Esters of the Tartaric Acids.*—The rotatory powers of the esters of the tartaric acids with the methyl-*n*-hexylcarbinols have been determined in the hope that the results might be useful in supporting the conclusions of Patterson (Trans., 1907, 91, 705) as to the non-validity of van't Hoff's theory of optical superposition. The rotatory powers observed were not in accordance with this theory, but owing to the failure of all attempts to prepare the corresponding esters of *i*-tartaric acid these results do not give a strict proof of its von-validity, such as Patterson has furnished in his work on the methyltartratos. McCrae has described ethyl  $\beta$ -octyl *d*-tartrate (Trans., 1901, 79, 1103) and di- $\beta$ -octyl *d*-tartrate (Trans., 1902, 81, 1221) as viscous oils with a rancid odour, and the latter as having a yellow colour. The esters mentioned

in table X have all been obtained as highly-refracting, colourless liquids, somewhat viscous and practically odourless. The preparation of the di- $\beta$ -octyl tartrates is readily carried out as follows: 40 grams of the required methyl- $n$ -hexylcarbinol and 10 grams of the diethyl ester of the tartaric acid are mixed and saturated at a temperature below 0° with hydrogen chloride. After some days, the hydrogen chloride and about 5 c.c. of the mixture are distilled off under diminished pressure on a water-bath. The main bulk of the mixture is then again saturated with hydrogen chloride as before, and kept for a week. The excess of alcohol, along with the hydrogen chloride, is now removed by distillation under a pressure of about 20 mm., and the ester carefully fractionated under a pressure of about 6 mm. One distillation is generally sufficient to give a product of constant rotation, the neutral esters boiling between 202° and 210°/6 mm.

In view of the discrepancy between McCrae's results and those here recorded, specimens of di- $\beta$ -octyl *d*-tartrate were prepared from Kahlbaum's alcohol (with a slight lavoration) and both diethyl and dimethyl *d*-tartrate, each preparation being found to have  $[\alpha]_D^{25} + 10.99^\circ$ , whereas McCrae's value is  $[\alpha]_D^{25} + 7.06^\circ$ . Similar preparations from the pure *dl*-alcohol and diethyl and dimethyl *d*-tartrates had  $[\alpha]_D^{25} + 11.18^\circ$  and  $+ 11.02^\circ$  respectively. In the preparation of these esters from Kahlbaum's alcohol it was found that the rotation of the unesterified alcohol varied slightly from that of the original sample. As purchased, it had, in a 2-dem. tube,  $\alpha - 0.14^\circ$  to  $- 0.17^\circ$ , whilst the unesterified alcohol had  $\alpha - 0.05^\circ$  to  $- 0.07^\circ$ . In the course of the lengthy series of experiments summarised on p. 48, ethyl *dl*- $\beta$ -octyl *d*-tartrate was isolated. It boils at 187—190°/7 mm., has  $d_4^{25} 1.0568$ , and  $[\alpha]_D^{25} + 8.55^\circ$ , a value higher than that recorded by McCrae (*loc. cit.*), who gives  $[\alpha]_D^{25} + 7.63^\circ$ .

Attempts to prepare the pure  $\beta$ -octyl esters of *i*-tartaric acid were failures, these compounds apparently decomposing before distillation.\*

TABLE X.  
*The Di- $\beta$ -Octyl Esters of the Tartaric Acids.*  
*Specific Rotatory Powers and Densities.*

	<i>d</i> -Tartaric acid.	<i>l</i> -Tartaric acid.	<i>r</i> -Tartaric acid.
<i>d</i> -Methyl- $n$ -hexylcarbinol, $[\alpha]_D^{25}$ ...	+ 21.06	+ 2.06	+ 14.12
	$d_4^{25}$ ..... 1.0165	1.0081	1.0047
<i>l</i> -Methyl- $n$ -hexylcarbinol, $[\alpha]_D^{25}$ ...	- 1.93	- 24.20	- 14.03
	$d_4^{25}$ ..... 1.0171	1.0059	1.0058
<i>dl</i> -Methyl- $n$ -hexylcarbinol, $[\alpha]_D^{25}$ ...	+ 11.02	- 11.00	-
	$d_4^{25}$ ..... 1.0143	1.0069	-

\* The authors are greatly indebted to Dr. M. O. Forster, F.R.S., who attempted to distil a sample of one of these esters. He found that violent decomposition set in at about 160° when the pressure was only 0.5 mm.

*Halides Corresponding with the Methyl-n-hexylcarbinols.*

*d*- and *l*-Methyl-n-hexylcarbinols react fairly readily with hydrogen iodide, bromide or chloride, the formation of the halide being accompanied by a change in the sign of the rotation. The  $\beta$ -iodo-octanes are obtained when the alcohols are saturated at  $0^\circ$  with hydrogen iodide and kept for about five hours. In the case of the bromides and chlorides, the mixtures similarly prepared are heated at  $100^\circ$  in sealed tubes for one hour.

These halides are partly racemised if the reactions are not carried out under the above conditions, higher temperatures or prolonged heating always resulting in the products formed being of lower rotatory power. All the preparations obtained were unaltered in rotatory power after prolonged shaking with cold concentrated sulphuric acid. These active halides do not appear to undergo autoracemisation, as a specimen of *l*- $\beta$ -bromo-octane was found to be unaltered in rotatory power two and a-half years after its preparation.

Various constants for these halides are given in table XI; the following additional ones were determined for *l*- $\beta$ -bromo-octane:  $d_4^{25}$  1.0927,  $\rho$  1.0805,  $\gamma$  1.0688, and  $\eta$  1.0532;  $[\alpha]_D -31.07^\circ$  at  $4^\circ$ ,  $-30.33^\circ$  at  $13.1^\circ$ ,  $-29.05^\circ$  at  $30^\circ$ ,  $-28.62^\circ$  at  $37.4^\circ$ ,  $-27.81^\circ$  at  $50^\circ$ ,  $-26.56^\circ$  at  $69^\circ$ , and  $-25.18^\circ$  at  $92^\circ$ .

TABLE XI.

*Halides from Methyl-n-hexylcarbinol.*

	Boiling point.	$d_4^{25}$ .	$\alpha_{D}^{25}$ in 50-mm. tube.	$\alpha_{D}^{25}$ in $\mu$ .
<i>d</i> - $\beta$ -Iodo-octane .....	101/22 mm.	1.3311	+26.51	+39.83 $^\circ$
<i>l</i> - $\beta$ -Iodo-octane .....	92/12 "	1.3299	-26.97	-40.56
<i>d</i> - $\beta$ -Bromo-octane ...	74/18 "	1.0895	+14.98	+27.33
<i>l</i> - $\beta$ -Bromo-octane ...	71/14 "	1.0814	-14.90	-27.47
<i>d</i> - $\beta$ -Chloro-octane ...	75/28 "	0.8658	+8.83	+20.10
<i>l</i> - $\beta$ -Chloro-octane ...	70/25 "	0.8628	-8.82	-20.44

Several experiments were carried out in which the halides were treated under varying conditions with potassium acetate. Although in every case the resulting  $\beta$ -octyl acetate had a rotation opposite in sign to the halide used, yet it was never obtained optically pure, some racemisation invariably taking place during the formation of the acetate, whilst possibly the halides themselves were not optically pure.

*d-Methyl-n-heptyl-, d-Methyl-n-octyl-, and d-Methyl-n-nonyl-carbinols.*

These were each prepared in two ways, namely, from the brucine and from the strychnine salts of the dextrorotatory hydrogen phthalic esters. The following constants were determined:

*d-Methyl-n-heptylcarbinol* boiled at 105°/19 mm., had  $d_4^{20}$  0·8281,  $\pi^{\text{D}}$  0·8202,  $\pi^{\text{H}}$  0·8129,  $\pi^{\text{S}}$  0·8043,  $\pi^{\text{B}}$  0·7799, and  $[\alpha]_D + 8\cdot98^\circ$  at 19°,  $+ 8\cdot88^\circ$  at 26·5°,  $+ 8\cdot71^\circ$  at 34°,  $+ 8\cdot55^\circ$  at 49·5°,  $+ 8\cdot44^\circ$  at 66°, and  $+ 8\cdot39^\circ$  at 72°.

*d-Methyl-n-octylcarbinol* boiled at 110—111°/11 mm., had  $d_4^{13}$  0·8293,  $\pi^{\text{D}}$  0·8220,  $\pi^{\text{H}}$  0·8096,  $\pi^{\text{S}}$  0·7935, and  $\pi^{\text{B}}$  0·7222, and  $[\alpha]_D + 8\cdot74^\circ$  at 17°,  $+ 8\cdot55^\circ$  at 26·4°,  $+ 8\cdot37^\circ$  at 35·4°,  $+ 8\cdot02^\circ$  at 58·9°,  $+ 7\cdot75^\circ$  at 93°, and  $+ 7\cdot81^\circ$  at 146°.

*d-Methyl-n-nonylcarbinol* boiled at 128°/20 mm. and solidified when cooled to a mass of stellate needles, which melted at 12°. It had  $d_4^{13}$  0·8318,  $\pi^{\text{D}}$  0·8236,  $\pi^{\text{H}}$  0·8145,  $\pi^{\text{S}}$  0·8017,  $\pi^{\text{B}}$  0·7896, and  $[\alpha]_D + 8\cdot40^\circ$  at 6°,  $+ 8\cdot18^\circ$  at 18°,  $+ 8\cdot03^\circ$  at 25·7°,  $+ 7\cdot88^\circ$  at 35°,  $+ 7\cdot67^\circ$  at 48·7°,  $+ 7\cdot55^\circ$  at 59°,  $+ 7\cdot34^\circ$  at 73°, and  $+ 7\cdot27^\circ$  at 92°.

*d-Methyl-n-decylcarbinol*, obtained from the brucine salt of the dextrorotatory hydrogen phthalic ester, boiled at 146°/24 mm., and, when cooled, set to a mass of stout, prismatic rods in a crystalline matrix. This melted at 18·7°, had  $d_4^{20}$  0·8369 (in a supercooled condition),  $\pi^{\text{D}}$  0·8263,  $\pi^{\text{H}}$  0·8182,  $\pi^{\text{S}}$  0·8090,  $\pi^{\text{B}}$  0·8016, and  $[\alpha]_D + 7\cdot80^\circ$  at 19°,  $+ 7\cdot66^\circ$  at 27°,  $+ 7\cdot51^\circ$  at 36·5°,  $+ 7\cdot32^\circ$  at 46·5°,  $+ 7\cdot15^\circ$  at 57·5°,  $+ 7\cdot00^\circ$  at 71°, and  $+ 6\cdot88^\circ$  at 93°.

*d-Methyl-n-undecylcarbinol*, obtained either from the brucine or strychnine salt of the dextrorotatory phthalic ester, boiled at 156—157°/17 mm., and set to a glistening, crystalline mass of prismatic needles, which melted at 30°. It had  $d_4^{20}$  0·8215,  $\pi^{\text{D}}$  0·8109,  $\pi^{\text{H}}$  0·8012, and  $[\alpha]_D + 7\cdot10^\circ$  at 25·5° (when supercooled),  $+ 6\cdot98^\circ$  at 33·5°,  $+ 6\cdot74^\circ$  at 48°,  $+ 6\cdot55^\circ$  at 56·5°,  $+ 6\cdot42^\circ$  at 71·9°, and  $+ 6\cdot37^\circ$  at 93°.

*d-Methylisobutylcarbinol* was obtained from the brucine salt of the dextrorotatory hydrogen phthalic ester and from the cinchonidine salt of dextrorotatory hydrogen succinic ester. It boiled at 65·5°/45 mm., had  $d_4^{\text{H}}$  0·8083,  $\pi^{\text{D}}$  0·8014,  $\pi^{\text{H}}$  0·7824,  $\pi^{\text{S}}$  0·7506, and  $[\alpha]_D + 21\cdot35^\circ$  at 6·3°,  $+ 20\cdot86^\circ$  at 14°,  $+ 20\cdot4^\circ$  at 21·3°,  $+ 20\cdot0^\circ$  at 29·5°,  $+ 19\cdot69^\circ$  at 38·7°,  $+ 19\cdot48^\circ$  at 43°,  $+ 19\cdot11^\circ$  at 57°,  $+ 18\cdot65^\circ$  at 72°, and  $+ 18\cdot25^\circ$  at 94·3°.

*l-Methylisobutylcarbinol*, obtained from the brucine salt of the levorotatory hydrogen succinic ester, had  $[\alpha]_D^{\text{H}} - 20\cdot80^\circ$ .

*d-Ethyl-n-hexylcarbinol*, obtained from the brucine salt of the dextrorotatory hydrogen phthalic ester, boiled at 97°/17 mm., had  $d_4^{\text{H,S}}$  0·8281,  $\pi^{\text{D}}$  0·8202,  $\pi^{\text{H}}$  0·8129,  $\pi^{\text{S}}$  0·8043,  $\pi^{\text{B}}$  0·7799, and  $[\alpha]_D + 8\cdot09^\circ$  at 61°.

$+8.05^\circ$  at  $20.6^\circ$ ,  $+8.13^\circ$  at  $37.8^\circ$ ,  $+8.14^\circ$  at  $48.2^\circ$ , and  $+8.27^\circ$  at  $70.5^\circ$ .

l-Ethyl-n-hexylcarbinol, obtained from the cinchonidine salt of the levorotatory hydrogen phthalic ester, boiled at  $94^\circ/13$  mm., had  $d_4^{25} 0.8277$ , and  $[\alpha]_D^{25} -7.96^\circ$ .

Table XII shows some of the properties of the  $\gamma$ -chloro-, bromo-, and iodo-nonanes, which were prepared by the methods used in the case of the corresponding  $\beta$ -octane derivatives. In each case the alcohol yielded a halogen derivative with a rotatory power of opposite sign.

TABLE XII.  
 $\gamma$ -Halogen Derivatives of n-Nonane.

	Boiling point.	$d_4^{25}$ .	$[\alpha]_D^{25}$ .
d- $\gamma$ -Chlorononane .....	87—89°/21 mm.	0.8588	+7.71°
l- $\gamma$ -Chlorononane .....	101°/40 ,	0.8549	-8.03
d- $\gamma$ -Bromononane .....	112°/32 ,	1.0800	+12.90
l- $\gamma$ -Bromononane .....	96—97°/22 ,	1.0897	-13.39
d- $\gamma$ -Iodononane .....	120°/27 ,	1.2940	+17.65
l- $\gamma$ -Iodononane .....	122°/37 ,	1.2873	-17.50

d-Phenylmethylcarbinol,  $C_6H_5\cdot CH(OH)\cdot CH_3$ , obtained from the brucine salt of the dextrorotatory hydrogen succinic ester, boiled at  $100^\circ/18$  mm., had  $d_4^{25} 1.0191$ ,  $d_4^{27} 1.0079$ ,  $d_4^{29} 1.0019$ ,  $d_4^{31} 0.9911$ ,  $d_4^{33} 0.9846$ ,  $d_4^{35} 0.9646$ , and  $[\alpha]_D$ ,  $+42.90^\circ$  at  $6^\circ$ ,  $+42.85^\circ$  at  $27^\circ$ ,  $+42.74^\circ$  at  $36.8^\circ$ ,  $+42.69^\circ$  at  $47^\circ$ ,  $+42.53^\circ$  at  $58^\circ$ ,  $+42.27^\circ$  at  $71^\circ$ , and  $+41.33^\circ$  at  $94^\circ$ .

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d-Phenylethylcarbinol, obtained from the brucine salt of the dextrorotatory hydrogen succinic ester, boiled at  $115—116^\circ/25$  mm., had  $d_4^{25} 0.9962$ , and  $[\alpha]_D^{25} +27.35^\circ$ .

l-Phenylethylcarbinol, obtained from the cinchonidine salt of the corresponding levorotatory ester, boiled at  $115—116^\circ/25$  mm., had  $d_4^{25} 0.9982$ ,  $d_4^{27} 0.9872$ ,  $d_4^{29} 0.9755$ ,  $d_4^{31} 0.9538$ , and  $[\alpha]_D$ ,  $-24.76^\circ$  at  $5.3^\circ$ ,  $-26.83^\circ$  at  $15.2^\circ$ ,  $-29.07^\circ$  at  $27.2^\circ$ ,  $-30.34^\circ$  at  $35^\circ$ ,  $-33.90^\circ$  at  $64.5^\circ$ , and  $-35.58^\circ$  at  $94^\circ$ .

The corresponding chloro-compounds were obtained when these three alcohols were saturated at  $0^\circ$  with hydrogen chloride and kept for some hours.

l-a-Chloroethylbenzene,  $C_6H_5\cdot CHCl\cdot CH_3$ , from the dextrorotatory carbinol, boiled at  $86^\circ/22$  mm., had  $d_4^{25} 1.0642$ , and  $[\alpha]_D^{25} -5.89^\circ$ .

The levorotatory phenylethylcarbinol yielded d a chloropropylbenzene, which boiled at  $86—87^\circ/15$  mm., had  $d_4^{25} 1.0429$ , and  $[\alpha]_D^{25} +3.79^\circ$ . The corresponding dextrorotatory chloro-compound boiled at  $95^\circ/25$  mm., and had  $d_4^{25} 1.0430$  and  $[\alpha]_D^{25} -3.87^\circ$ .

The authors have much pleasure in acknowledging the assistance given to them by Miss Annie Higson, B.Sc. (Lond.), who prepared and

carried out many experiments with methylmethylethylcarbinol, and by Mr G. T. Byrne, B.Sc. (Manc.), who has repeated several of the resolutions described.

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MUNICIPAL TECHNICAL SCHOOL,  
BLACKBURN.

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### VIII.—*The Chemistry of Mesothorium*

By FREDERICK SODDY, M.A., F.R.S.

MESOTHORIUM, the first product of the thorium disintegration series, and the parent of radiothorium, was discovered three years ago by O. Hahn (*Ber.*, 1907, **40**, 1482). Although for the past few months powerfully radioactive preparations of this substance, prepared by Hahn during the course of the manufacture of thorium salts from monazite sand in the works of Dr. Knöslér & Co., Plotzensee, Berlin, have been put on the market, nothing has been allowed to transpire concerning the chemical processes by which the separation is effected. Rutherford, in a Royal Institution Lecture (January 31st, 1908), drew attention to the value of mesothorium as a possible substitute for radium in many experiments, owing to the large scale on which thorium compounds are commercially manufactured. Although mesothorium is not a permanent source of radioactivity, like radium practically is, yet the period of average life, about eight years, is sufficiently long to make it a very useful substance if it could be prepared on a large scale. At the beginning of the present year, powerful sources of thorium radioactivity were needed for certain experiments, and as at that time there seemed no possibility of obtaining it in any other way, experiments were undertaken on the separation of mesothorium from thorium minerals, commencing with thorianite.

The discovery of radiothorium by Sir William Ramsay and O. Hahn, which preceded that of mesothorium, was made in the course of the treatment of a large quantity of thorianite for radium. The material was fused with potassium hydrogen sulphate, the insoluble residue being treated in the same way as the radium.

\* Since this paper was written there has appeared a communication on the same subject by W. Marckwald (*Ber.*, 1910, **43**, 3420) which anticipates the discovery of the chemical identity of mesothorium-1 and radium.

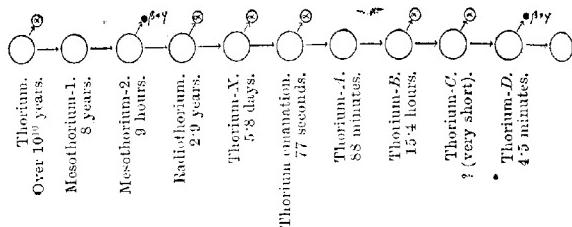
containing residues from pitchblende, to extract the barium as chloride. Radiothorium was discovered in this product (Sir W. Ramsay, *J. Chim. Phys.*, 1905, **3**, 617; O. Hahn, *Jahrb. Radioaktiv. Elektronik*, 1905, **2**, 234). Subsequently a study of the chemical properties of radiothorium by Elster and Geitel (*Physikal. Zeitsch.*, 1906, **7**, 445) and G. A. Blanc (*Phil. Mag.*, 1905, [vi], **9**, 148), and the work of Boltwood (*Amer. J. Sci.*, 1907, [iv], **25**, 93), resulted in the view at present held, that radiothorium resembles thorium completely and cannot be separated from it by chemical processes, and that the radiothorium prepared by Hahn was due to the separation of mesothorium and the spontaneous production of radiothorium from it with the lapse of time. What little is known of the chemistry of mesothorium we owe to Boltwood, who showed that the original process employed in the separation of thorium-X (Rutherford and Soddy, *Trans.*, 1902, **81**, 343, 837) in the filtrate after precipitation of thorium by ammonia, separated also the mesothorium. He also precipitated barium sulphate in a dilute solution of a thorium salt, thinking that the adsorption of radiothorium by the barium sulphate might explain Hahn's results with thorianite. He found, however, that mesothorium, but not radiothorium, was separated with the barium sulphate, and concludes: "It appears quite likely therefore that the entraining action of barium sulphate on mesothorium was directly responsible for the presence of radiothorium in the thorianite residues [of Hahn]." Since Sir W. Ramsay and Hahn were dealing with a mixture of radiothorium and mesothorium in genetic relationship, nothing can be learnt from the original papers on radiothorium (*loc. cit.*) of the chemistry of mesothorium,\* as it is uncertain throughout to which substance the reactions apply, whilst in Hahn's later papers on mesothorium (*loc. cit.*, and *Physikal. Zeitsch.*, 1907, **8**, 277) no information on this subject is given.

Thorianite is, from the radioactive point of view, the most complex material it is possible to work with, as it contains every one of the thirty or more radioactive elements known, in important quantity, the penetrating radiation contributed by the uranium and thorium series being, for the specimen of thorianite examined (which contained about three times as much thorium as uranium), of very similar intensity. The thorium disintegration series, as at present known, is shown below to facilitate reference, and no phenomena were encountered in the course of the work which could

\* Thus Sir W. Ramsay, for example, in his paper "Radio-thorium" (*J. Chim. Phys.*, 1905, **3**, 623) says, "Le nouveau corps se précipite partiellement avec le radium, en ajoutant aux sels de thorium d'abord un sel de baryum et ensuite de l'acide sulfurique ; et l'on peut effectuer sa séparation du radium par un des procédés dont nous avons donné la description."

not readily be explained by this succession of changes and by the known changes in the radium series.

Throughout,  $\gamma$ -ray methods of measurement with lead electroscopes (Soddy and Russell, *Phil. Mag.*, 1910, [vi], **19**, 752) have been employed whenever possible, as by these means the difficulty of comparing together specimens differing greatly in density and weight is avoided. The only objection to it is that considerable amounts of material must be employed to produce effects sufficiently large to measure with accuracy. In dealing with monazite, a special very large lead cylindrical electroscope (32 cm. high and 22 cm. diameter) was constructed so as to give greater sensitiveness. The lead used, which was 3 to 4 mm. thick, was taken from the roof of a very old building, in which any radio-lead initially present would have decayed (*Ann. Reports*, 1906, **3**, 365), so that the natural leak might be as small as possible. It proved very successful. A very



complete study of the  $\gamma$ -radiation of the various radio-elements, in conjunction with Mr. Russell, has recently been concluded, and the section dealing with the  $\gamma$ -rays of thorium has appeared in the *Philosophical Magazine* (1911, [vi], **21**, 130). It suffices to state here that the two thorium types of  $\gamma$ -rays, from mesothorium-2 and thorium-*D*, both in penetrating power and in the ratio of their intensity to that of the accompanying  $\beta$ -rays, are extremely similar to the radium type of  $\gamma$ -rays which are given by radium-*C*. Radium-*C*, mesothorium-2, and thorium-*D*, alone of all the known radioactive constituents, give  $\gamma$ -radiation of sufficient intensity to affect the measurements. When  $\beta$ -ray methods are employed, the possible effects due to uranium-*X*, radium-*E*, and, perhaps, actinium-*C* must also be remembered, but the  $\gamma$ -rays from these substances are negligible. In all measurements of  $\gamma$ -rays, the preparations were contained in sealed test-tubes, so as to retain the radium emanation completely. In spite of the complexity of thorianine, no difficulty was ever experienced in deducing from the variations of the  $\gamma$ -activity with time the radioactive constituents present and their relative amount, although two of the periods

(those of the radium emanation and thorium-X) controlling the  $\gamma$ -ray variations are identical.

For the specimen of thorianite worked with, moreover, the  $\gamma$ -activity contributed by thorium-D was very similar in intensity to that contributed by radium-C, so that, frequently, preparations appeared to remain of constant activity for long periods, when what was really taking place was a simultaneous complete decay of thorium-X (and in consequence thorium-D) and a concomitant reproduction of radium emanation (and in consequence radium-C) from the radium. The analysis of the effects was no doubt enormously simplified, because, as will appear in the sequel, mesothorium-1, radium, and thorium-X appear to form a trio of chemically non-separable elements.

Experiments were started with a solution of thorianite in nitric acid by the two known methods, capable of separating mesothorium, due to Boltwood. The repeated precipitation of the solution with ammonia and evaporation and ignition of the filtrate, as in the preparation of thorium-X, effects a complete separation in sufficiently dilute solution, but in an attempt to apply it to considerable quantities with more concentrated solutions, the separation was partial, and the fraction separated varied capriciously. The precipitation in the thorianite solution of barium as sulphate, although at first not very successful, was found ultimately, under proper conditions, to yield good results, even in concentrated solutions the separation being nearly complete. In one experiment 26 grams of barium nitrate was dissolved in a solution of 600 grams of thorianite in nitric acid, from which most of the excess of acid had been evaporated. The solution, of volume about 1.5 litres, was put in a Winchester quart bottle, excess of dilute sulphuric acid added, and the bottle shaken for an hour on a shaking machine. The separation of the mesothorium was practically complete, a second precipitation yielding a precipitate possessing an activity not greater than could be accounted for by the regeneration of thorium-X in the time between the precipitations.

About 5 kilograms of thorianite were treated by this method, and the  $\gamma$ -activity of the products, sealed up in test-tubes, was kept under observation for some time. The first precipitate from the solution increased rapidly in  $\gamma$ -activity by about 50 per cent. in the course of two days, and then remained nearly constant. During filtering and drying, mesothorium-2 is usually produced in nearly equilibrium amount before the first measurement. The increase for the first two days is due to the formation of thorium-D from thorium-X. After that time the decay of thorium-X just balanced the production of radium-C from the radium as already explained,

so that the activity remains sensibly constant. For the subsequent precipitates the  $\gamma$ -activity was due mainly to thorium-*X*, regenerated between the precipitations, and, after reaching the maximum, steadily decayed.

In this way, from the 5 kilograms of thorianite a total weight of about 200 grams of barium sulphates of various activities was separated. Up to this time it was considered, as Boltwood had supposed, that the mesothorium was merely adsorbed by the barium sulphate. Uranium-*X* was, in a recent research (F. Soddy and A. S. Russell, *Phil. Mag.*, 1909, [vi], 18, 620), frequently separated by adsorption with barium sulphate, and was found to be readily separable from the barium after solution of the barium sulphate, by precipitating with ammonia in presence of a trace of iron.

In the hope of being able to effect a preliminary concentration of the mesothorium from the barium, to a portion of one of the sulphate precipitates, after conversion into chloride, a small quantity of dilute sulphuric acid was added to precipitate a small fraction of the barium as sulphate. The precipitate so obtained, however, was no more and no less active than the same weight of original material. Other attempts to concentrate the mesothorium from the barium, chemically, failed, and the conclusion was drawn that the separation of mesothorium with barium is due, not to an adsorption by the barium sulphate, as had previously been assumed, but to a chemical resemblance between the two elements.

The whole of the active barium sulphate was converted into chloride by ignition with sugar-carbon in separate small quantities in quartz crucibles, and the barium sulphide dissolved in hydrochloric acid. The crude chlorides in acid solution were freed from lead by hydrogen sulphide, made alkaline with ammonia, and filtered from the small iron and thorium hydroxide precipitate. A fractional crystallisation of the barium chloride was then commenced to concentrate the radium present from the barium. The various precipitates had been sorted into three grades, according to their activity, and worked up into pure chlorides separately. The raw material for the fractionations thus comprised three preparations of weights 52, 69, and 105 grams, and relative activities roughly as 5 : 2 : 1. As it was then unknown whether the separation of the barium from the mesothorium would be possible, the fractions were not mixed, but dissolved separately. Fractionation was carried out for separating radium from barium in the usual way, the mother liquor of the richer fraction being used to dissolve the crystals of the next richest. Preliminary tests showed that the process was very effective in concentrating the mesothorium as well as the radium from the barium. In a few days three fractions were

again made up, of weights 57, 97·5, and 76·5 grams. Mesothorium-2 was separated from each separately by adding 10 milligrams of thorium nitrate, and precipitating with ammonia. The relative activities of these mesothorium-2 precipitates were as 25·3 : 4·3 : 1. The mesothorium in equal weights of barium chloride was therefore as 34 : 3·4 : 1. This showed that the mesothorium had been effectively concentrated by the fractional crystallisation, the crystals being enriched, and the mother liquor impoverished, as in the case of radium. The three fractions were dissolved, left for a week, then evaporated to dryness and sealed up in test-tubes, and the  $\gamma$ -activity measured over a period of six weeks, 10 grams only of the first fraction being taken for the test. The ratio between the initial and subsequently generated activity gives the relative proportions of mesothorium and radium. These ratios were in order of richness of the preparation, 0·52, 0·46, and 0·56. Hence mesothorium follows the radium extremely closely in the fractionations. The small differences in the ratio, since the raw material of the fractionations was not homogeneous, but derived from different quantities of thorianite, are not greater than might be accounted for by variations in the composition of the mineral, or by the presence, possibly, of thorium-X from regenerated radiothorium. The measurements were only rough, whereas those which follow were done with the greatest possible accuracy.

In order to settle whether any alteration at all in the proportion of the mesothorium and radium was produced by fractional crystallisation, the most active fraction, all but the 10 gram sample sealed up for the previous tests, was refractionated as before. The richest fractions, withdrawn from the process after the fifth and eighth successive fractionations, were combined and labelled A.1. A part of the 10 gram sample of the original material was taken, and labelled .1. The two specimens were dissolved in water at the same time, freed from mesothorium-2 by precipitation of thorium hydroxide in the solution as before, evaporated, and sealed up. A weighed 2·38 grams, and A.1 2·09 grams. The  $\gamma$ -rays were compared after two days, when mesothorium-2 is again in equilibrium, and at intervals subsequently. The measurements give the means of telling exactly whether any alteration in the ratio of the radium and mesothorium has been effected by the further fractionation.

Fraction A.1 proved to be 8·75 times as active as fraction .1, showing that a concentration of the active material in the ratio 10 : 1 had been effected. Nevertheless, the proportions of radium and mesothorium in the two preparations were identical. The ratio of the activities remained unchanged within the error of

measurment, which may be estimated at less than 2 per cent., over the period from the first day after preparation onward, during which the activity more than doubled, owing to the accumulation of the radium emanation. In order to more accurately compare the two preparations, measurements were taken not only of the two in the same position beneath the electroscope, but also of the stronger preparation at a greater distance, so that the effects compared should be of the same order. The following table shows the actual readings of the electroscope in divisions per minute, corrected for the natural leak (about 4·8), and the ratio between them for the two positions.

Day.	Fraction A.	Fraction AA.		Ratios.	
		91·5	12·06	8·7	1·14
1st.....	10·5				
2nd.....	13·1	115·0	14·95	8·8	1·14
3rd.....	15·0	133·0	17·35	8·85	1·15
7th.....	19·65	170·8	22·3	8·7	1·13
13th.....	23·9	203·0	26·6	8·5	1·12
34th.....	26·0	224·0	29·5	8·6	1·14

The fractionation process, from which the fraction *AA* was derived, was continued until twenty-four sets of fractionations had been performed. The products were then combined in two final fractions, the one, labelled *C*, consisting of the weak, and the other, labelled *B*, of the rich fractions. Thus the most active fraction of the original material was obtained in three fractions, *AA*, *B*, and *C*, the weights of which were 2·09, 2·27, and 38 grams respectively, and the relative activities as 4·6: 3·85: 1. The concentrations of the radioactive matter in the three fractions were therefore as 84: 64: 1. Fractions *B* and *C* were kept dissolved in water for some days, so that mesothorium-2 should be initially in equilibrium, then evaporated to dryness, sealed up in test-tubes, measured immediately, and again after twenty-one days. The relative activity of the two fractions was exactly the same in the two tests, showing that the fractionation process which had altered the concentration of the radioactive matter sixty-two times had not affected the ratio of the two radioactive constituents. For each fraction the proportion of the activity contributed by the mesothorium was almost exactly one half that contributed by the radium, which is practically the same as that found initially.

This experiment proves conclusively therefore that in the fractional crystallisation of barium chloride, containing mesothorium and radium, the mesothorium and radium behave as a single substance, and there is no hope of separating them by this method.

With the knowledge gained of the chemical nature of mesothorium, a good many further experiments were done on its

separation from thorianite, which need not be detailed. They all bore out the view that mesothorium and barium are chemically analogous. It was found that a practically complete separation of the mesothorium and radium from thorium in the thorianite solution could most favourably be effected by adding a small quantity of barium nitrate and a considerable quantity of strong nitric acid, and precipitating the thorium with oxalic acid in the strongly acid solution. The mesothorium is precipitated from the filtrate by pouring it into excess of sodium carbonate solution (which keeps the uranium dissolved), and recovered from the solution of the precipitate in nitric acid by precipitating the barium with sulphuric acid.

In the first experiment with monazite sand, 400 grams were dissolved, by heating it with twice its weight of sulphuric acid and stirring the product with cold water, exactly as in the technical working up of the material. The muddy liquor obtained was decanted from the unattacked sand, which constituted about 20 per cent. of the whole, and left to deposit its sediment. This weighed 4·8 grams, and consisted largely of calcium sulphate. It was labelled *A*. One gram of barium nitrate was dissolved, and added slowly to the clear monazite solution, with efficient stirring. The precipitate (labelled *B*) weighed 1·8 grams. Tested by  $\gamma$ -ray methods, the undissolved sand retained about 4·5 per cent. of the total activity of the material. The  $\beta$ -activities of the sediment *A* and precipitate *B* were as 1 to 3 initially, and as 1 to 2 after forty days. Thus, under the ordinary conditions of the thorium manufacture, an important part of the mesothorium is lost in the insoluble sediments. The chemical behaviour of mesothorium, as is to be expected, is indefinite in the absence of sufficient barium to be quantitatively separable. Monazite contains much less uranium and therefore radium, relatively to thorium, than thorianite, and the  $\gamma$ -rays of the preparation *B* in consequence fell to about half its maximum value in the course of a month, owing to the effect of the decay of thorium-*X* exceeding the growth of radium-*C*.

Further experiments with 400 and 800 grams of monazite sand were made as before, except that about 0·1 per cent. of barium carbonate was mixed with the sand before heating. The sediment obtained from the muddy solution now contained practically all the mesothorium and radium in the monazite. One such sediment, from 800 grams of monazite sand, weighed 14·5 grams and contained practically the whole of the mesothorium in the material. Its  $\gamma$ -ray activity at the maximum, three days after preparation, was about 70 per cent. of that of the original material. The unattacked sand retained 8 per cent. A further precipitate of 1·6 grams of

barium sulphate formed in the clear monazite solution possessed a small initial activity, due to regenerated thorium-*X* only, which almost completely decayed in the course of a month. Certainly less than 5 per cent. of the mesothorium in the sediment was present. As throughout the work thorium-*X*, mesothorium, and radium have always been separated together, the presence of thorium-*X* and absence of mesothorium in this precipitate may be regarded as clear evidence that practically the whole of the mesothorium can be separated from monazite by the method described. The  $\gamma$ -radiation of the main sediment fell to about 57 per cent. of its maximum value after a month, as the effect of the decay of thorium-*X* overpowers the increase due to the generation of radium-*C*.

In the course of two or three years it is to be expected that the preparation will rise in activity to somewhat more than its initial value, due to the regeneration of radiothorium, and in consequence thorium-*X* (and also of radium-*C*, which does not contribute to the initial activity). Then it will decay exponentially, with the period of mesothorium-1, to the constant small proportion contributed by the radium.

A part of this sediment was boiled with sodium carbonate, washed free from sulphates, and dissolved in hydrochloric acid. It left an inactive residue, mainly silica, whilst from the solution practically the whole of the radioactive matter was precipitated with the barium chloride by saturating it with hydrogen chloride. This is further evidence of the resemblance between mesothorium and radium. All the methods effective in the concentration of the latter which were tried serve equally well for mesothorium.

In going over all the measurements, which refer to more than thirty preparations, the activity of which was kept under observation for a month or longer, there is clear evidence also that thorium-*X* is always separated in any chemical operation in the same proportion as mesothorium and radium. It appears that the behaviour observed by Boltwood for the one reaction, precipitation with ammonia, is general. Certain apparent exceptions shown in the preparations measured were found, on referring back to the details of the separation, to be due to a lapse of time after the thorium-*X* had been separated from the mineral before the first measurement. In these circumstances, owing to the decay of the thorium-*X* after separation, its proportionate activity compared with that of mesothorium and radium appears low. Although no separate examination of the point has been made, there is good reason to believe that mesothorium, radium, and thorium-*X* are a chemically inseparable trio. It should be mentioned, however, that

G. Hoffmann (*Physikal. Zeitsch.*, 1907, **8**, 553), from a comparison of the coefficient of diffusion and ionic mobility of thorium-X in solution, deduced from Nernst's theory that the thorium-X ion is singly charged, and is therefore univalent. The conditions under which the radioactive measurements were carried out, however, were very far from definite. In the more recent work of Strömholt and Svedberg (*Zeitsch. anorg. Chem.*, 1909, **61**, 338; **63**, 197), some important additions have been made to the chemistry of the radio-elements. The method employed was new and ingenious. By crystallising various salts in solutions containing radioactive constituents, they sought to determine to which of the known elements the radio-elements were isomorphous. They concluded that no differences existed, even from the quantitative point of view, between thorium-X, actinium-X, and radium. So far as thorium-X is concerned, this agrees perfectly with the results given in this paper. They point out that in the thorium, actinium, and uranium-radium series the three emanations are identical chemically, being members of the family of inert gases. The preceding members, thorium-X, actinium-X, and radium, are again identical, all being members of the alkaline earth family. Next to these come radio-thorium, radioactinium, and ionium, which are all similar, but they are inclined to put in the Periodic Table the respective groups ionium, uranium-X, radio-uranium; radioactinium, actinium; and radiothorium, mesothorium, thorium, as analogous to the rare-earth group lanthanum to ytterbium, as follows:

	0.	1.	2.	3-4.
5th Period .....	Xe	Cs	Ba	La-Yb
	RaEm	--	Ra	Ionium (UX, RaU)
6th Period .....	{	AeEm	--	{
	ThEm	--	ThX	HaAc, Ac
				HaTh, M <sub>2</sub> Th, Th
				}
				U

Their work on mesothorium is indefinite and in disagreement, for the most part, with the results in this paper, that mesothorium-1 is identical chemically with radium and thorium-X. For example they state that ammonia precipitates all elements of the thorium series except thorium-X, and that mesothorium is not precipitated, like radium, along with barium sulphate, citing in support of this last some experiments, which, in their second paper, they withdraw because they have not been able to repeat them. It is clear that the chemical identity of mesothorium with radium completely negatives the above attempt to bring the radio-elements into the Periodic Table. The elements radiothorium, mesothorium, thorium suggest anything rather than the rare-earth group lanthanum to ytterbium.

It appears that chemistry has to consider cases, in direct  
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opposition to the principle of the Periodic Law, of complete chemical identity between elements presumably of different atomic weight, and no doubt some profound general law underlies these new relationships. Apart from the case of the three emanations, for which chemical identity is necessarily a common property of the whole group, we have, in addition to the case of radiolead (210·4) and lead (207·1), which are chemically inseparable, two well-defined groups of triplets: (1) Thorium (232·4), Ionium (230·5), Radio-thorium (228·4); (2) Mesothorium-1 (228·4), Radium (226·4), Thorium-X (224·4), in which the chemical similarity is apparently perfect. The atomic weights, estimated, for the unknown cases, by subtracting from the atomic weight of the parent substance the known number of helium atoms expelled in their formation, show a regular difference of two units between the successive members of these two groups. The first group consists of quadrivalent elements of the fourth vertical column and the second of bivalent elements of the second column of the Periodic System, and yet the atomic weight of the last member of the first, and first member of the second, group are, as far as is known, the same.

The chemical identity of the members of the above two groups is almost certainly much closer than anything previously known. In the rare-earth group, elements with neighbouring atomic weights are often so closely allied that they can only be separated after the most laborious fractionation, and distinguished by the difference in their equivalents. But as the latter are always very close, the test is a very rough one in comparison with what is possible for radio-elements. Take, for example, the case of ionium and thorium. Boltwood, Keetman, and, lastly, Auer von Welsbach have all failed completely to concentrate ionium from thorium, the latter after a most exhaustive examination, in which his unrivalled knowledge of the rare-earths was supplemented by the new, powerful methods of radioactive analysis (*Mitteilungen der Radium Kommission*, VI, *Sitzungsber. K. Akad. Wiss. Wien*, 1910, **119**, ii, a, 1). The question naturally arises whether some of the common elements may not, in reality, be mixtures of chemically non-separable elements in constant proportions, differing step-wise by whole units in atomic weight. This would certainly account for the lack of regular relationships between the numerical values of the atomic weights.

The examples given include all the known radio-elements with periods of average life longer than a year, except uranium,\* whilst for this element the fact that it alone gives two  $\alpha$ -particles per atom disintegrating, which probably are not derived from two

\* Actinium can hardly be considered in this connexion as its chemistry is still relatively imperfectly known.

rapidly succeeding changes on account of the lowness of their range, is good ground for considering that uranium may also be a mixture of two chemically non-separable elements in constant proportion due to their genetic relationship, differing in atomic weight by four units. On this view, uranium may be analogous to thorium and radiothorium, except that there is no intermediate product of different chemical nature to reveal their separate identities.

It is natural that relationships such as these, even if they were general, should at first appear to be confined to the longer-lived radio-elements. For the shorter-lived substances, not only on account of the evanescent character of the material is it difficult to determine their true chemical nature. Adsorption plays a much larger part in the separation of the short-lived products than it does in the case of the longer-lived. The reason is not far to seek. Radioactivity is a function, not of mass, but of mass divided by the period of average life. Thus a given amount of an adsorbent may be able to adsorb similar amounts of two radioactive substances before becoming saturated. If, however, the one is much longer lived than the other, when quantities, not equal, but possessing similar radioactivity are acted on, the separation may be practically complete for the shorter-lived substance, and for the other practically inappreciable.\* Polonium, although its period of average life is less than a year, has well-defined chemical properties, which have been elucidated by the exhaustive investigations of Mme. Curie and Marekwald. It will be interesting to see whether it does not prove to be identical with the still non-isolated "di-tellurium" of Mendeléeff, for the existence of which some recent evidence is forthcoming (W. R. Flint, *Amer. J. Sci.*, 1910, [iv], **30**, 209). It would at least be interesting to apply to the supposed mixtures of tellurium and di-tellurium the methods used by Marekwald in separating polonium from tellurium.

I desire to acknowledge the capable assistance of Mr. W. T. Munro in the preparation of the purified active barium chloride from thorianite.

PHYSICAL CHEMISTRY LABORATORY,  
UNIVERSITY OF GLASGOW,

\* This point of view also explains at once the remarkable observation of Ritzel (*Zeitsch. physikal. Chem.*, 1909, **67**, 725) that a trace of thorium sulphate completely prevents the adsorption of uranium-X by charcoal. For, according to Marekwald and Keetman, uranium-X is completely analogous chemically to thorium and cannot be separated from it.

IX.—*Attempts to Prepare Glycerides of Amino-acids.*

By ROMAN ALPERN and CHARLES WEIZMANN.

THE intention of the authors in commencing this work was to prepare glycerides of the simple amino-acids, for example, triaminotriacetin,  $\text{NH}_2\text{CH}_2\text{CO}\cdot\text{O}\cdot\text{CH}(\text{CH}_2\cdot\text{O}\cdot\text{CO}\cdot\text{CH}_2\cdot\text{NH}_2)_2$ , since in all probability substances of this nature would possess great physiological importance.

The direct combination of glycerol and glycine was found to be impossible, and while experiments in this direction were proceeding, Abderhalden (*Zeitsch. physiol. Chem.*, 1910, **65**, 53) published the results of experiments on the same lines, from which he drew the same conclusion.

The combination of  $\alpha$ -halogen substituted acids with glycerol was then carried out, with the idea of subsequent displacement of the halogen by the amino-group.

EXPERIMENTAL.

*Preparation of Trichlorotriacetin.*

It was found that the preparation could be carried out conveniently in two ways:

(1) Direct condensation of chloroacetic acid and glycerol by means of zinc chloride:

Chloroacetic acid (3 mols.), freshly distilled, is dissolved in glycerol (1 mol.). To this mixture is added zinc chloride (3 mols.), and the whole is heated on the water-bath for five hours. Water is then added, the trichlorotriacetin extracted with ether, the ethereal solution washed with water, then with sodium carbonate solution, dried, and distilled. The yield is 60 per cent. of the theoretical.

*Trichlorotriacetin* is a colourless, viscid oil, with a bitter taste; it boils at 205—208°/10 mm.:

0·1098 gave 0·1334  $\text{CO}_2$  and 0·0376  $\text{H}_2\text{O}$ . C=33·1; H=3·8.  
0·1526 „ 0·2050  $\text{AgCl}$ . Cl=33·0.

$\text{C}_9\text{H}_{11}\text{O}_6\text{Cl}_3$  requires C=33·5; H=3·4; Cl=33·0 per cent.

By condensing glycerol with bromoacetic acid in molecular quantities in an exactly similar manner,  $\alpha$ -monobromoacetin,  $\text{OH}\cdot\text{CH}_2\cdot\text{CH}(\text{OH})\cdot\text{CH}_2\text{O}\cdot\text{CO}\cdot\text{CH}_2\text{Br}$ , is obtained. This is a yellow oil, possessing a bitter taste, and boiling at 217—219°/10 mm.:

0·1555 gave 0·1670  $\text{CO}_2$  and 0·0560  $\text{H}_2\text{O}$ . C=28·4; H=4·0.  
 $\text{C}_9\text{H}_{9}\text{O}_4\text{Br}$  requires C=28·1; H=4·2 per cent.

(2) By the action of dry hydrogen chloride on a mixture of glycerol and either chloroacetyl chloride or chloroacetic anhydride:

Dry hydrogen chloride is passed into a mixture of glycerol and either chloroacetyl chloride or chloroacetic anhydride until, in the first case, a homogeneous, viscous mass is obtained, and, in the second, two layers separate. Water is then added, and the trichlorotriacetin isolated as before.

This method is also applicable to the preparation of triacetin, a very good yield being obtained.

*αα'-Dipropionin.*

Propionic anhydride (2 mols.) and glycerol (1 mol.) are condensed as described above. A colourless, mobile liquid is obtained in 45 per cent. yield, which possesses an aromatic odour, but also recalls that of propionic acid. It boils at 170—173°/10 mm.:

0·1174 gave 0·2264 CO<sub>2</sub> and 0·0826 H<sub>2</sub>O. C=52·6; H=7·8.

C<sub>9</sub>H<sub>16</sub>O<sub>5</sub> requires C=52·9; H=7·8 per cent.

The displacement of the halogen in trichlorotriacetin by the amino-group was not found possible under the conditions employed.

Dry gaseous ammonia, even at 0°, hydrolyses the ester with the production of glycol and chloroacetamide.

On boiling trichlorotriacetin in xylene solution with potassium phthalimide, reaction evidently took place. There was an abundant separation of potassium chloride, but from the viscous mass left by the evaporation of the xylene, nothing definite except phthalimide could be isolated.

*αα'-Diacetoacetin, OH·CH(CH<sub>2</sub>·O·CO·CH<sub>2</sub>Ac)<sub>2</sub>.*

In the hope of obtaining β-amino-derivatives of the glycerides, αα'-diacetoacetin was prepared by condensing ethyl acetoacetate with glycerol by means of concentrated sulphuric acid.

To a mixture of glycerol (10 grams) and ethyl acetoacetate (30 grams), 40 to 50 drops of concentrated sulphuric acid are added very slowly with constant shaking. After ten minutes, the two layers should have disappeared, and warming gently to about 50° facilitates this. If the layers do not now mix, a few more drops of sulphuric acid are added. The mixture is then kept for twelve hours; after it has been extracted with ether, the yellow ethereal solution is washed with a little water, dried, and distilled:

0·0926 gave 0·1762 CO<sub>2</sub> and 0·0666 H<sub>2</sub>O. C=51·7; H=7·9.

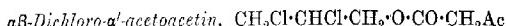
C<sub>11</sub>H<sub>16</sub>O<sub>5</sub> requires C=52·9; H=7·8 per cent.

αα'-Diacetoacetin is a viscid, yellow oil, boiling at 157—160°/14 mm., with an odour resembling that of ethyl acetoacetate. It is

insoluble in sodium carbonate solution, and gives a reddish-brown coloration with ferric chloride.

An attempt was then made to condense  $\alpha\alpha'$ -diacetoacetin with ethyl glycine (compare Fischer, *Ber.*, 1901, **34**, 433).

A very small quantity of a substance was obtained, which was neither the product of condensation of  $\alpha\alpha'$ -diacetoacetin and ethyl glycine nor diketopiperazine, but the amount was too small to permit of further investigation.



If, instead of concentrated sulphuric acid, a stream of dry hydrogen chloride is used as a condensing agent,  $\alpha\beta$ -dichlorohydrin condenses with ethyl acetoacetate to form  $\alpha\beta\text{-dichloro-}\alpha'\text{-acetoacetin}$ , which is a yellow oil, boiling at  $103\text{--}105^\circ/14$  mm.:

0·1230 gave 0·1778 CO<sub>2</sub> and 0·0554 H<sub>2</sub>O. C=39·4; H=4·9.  
C<sub>7</sub>H<sub>10</sub>O<sub>3</sub>Cl<sub>2</sub> requires C=39·4; H=4·6 per cent.

#### N-Allylglycine and its Ethyl Ester.

Attempts were also made to combine various derivatives of glycerol with ethyl glycine.

Epichlorohydrin, dichlorohydrin, and aerolein did not condense with ethyl glycine under all the conditions employed by the authors.

Allylamine, however, readily condenses with ethyl bromoacetate to form *ethyl N-allylglycine*, CH<sub>2</sub>·CH·CH<sub>2</sub>·NH·CH<sub>2</sub>·CO<sub>2</sub>Et.

The condensation is carried out as follows. The calculated quantity of allylamine is added to ethyl bromoacetate in ethereal solution in small quantities at a time, the whole being cooled to 0°. At the end of an hour a 33 per cent. solution of sodium hydroxide is added, and then dry potassium carbonate until the aqueous layer acquires a syrupy consistency. This is extracted several times with ether, the ethereal solution dried, and distilled. The ester boils at 75°–78°/15 mm.:

0·0586 gave 0·1248 CO<sub>2</sub> and 0·0198 H<sub>2</sub>O. C=58·1; H=9·4.

0·1383 „ 11·5 c.c. N<sub>2</sub> at 19° and 756 mm. N=9·5.

0·1184 „ 10·1 c.c. N<sub>2</sub> „ 18° „ 756 mm. N=9·8.

C<sub>7</sub>H<sub>13</sub>O<sub>2</sub>N requires C=58·7; H=9·1; N=9·8 per cent.

The best yield of the corresponding acid was obtained by hydrolysing the ester with methyl-alcoholic barium hydroxide. The barium is precipitated as sulphate, and the filtrate evaporated to dryness in a vacuum. The residue is extracted with water, and the solution evaporated to dryness in a vacuum. The product,

*N-allylglycine*, separates from methyl alcohol as a colourless, crystalline powder, melting at 158—159°:

0·1189 gave 12·8 c.c. N<sub>2</sub> at 15° and 752 mm. N=12·47.

C<sub>5</sub>H<sub>9</sub>O<sub>2</sub>N requires N=12·17 per cent.

In order to obtain a characteristic derivative of the acid, both the  $\alpha$ - and  $\beta$ -naphthalensulphonyl derivatives were prepared.

*N- $\alpha$ -Naphthalenesulphonylallylglycine* was prepared in the usual way. It is precipitated as an oil, which solidifies only after some days. It does not crystallise well from water.

*N- $\beta$ -Naphthalenesulphonylallylglycine* was also prepared. It is precipitated as an oil, which solidifies in a short time. It crystallises from water in colourless, glistening plates, melting at 131—132°:

0·1320 gave 0·2841 CO<sub>2</sub> and 0·0585 H<sub>2</sub>O. C=58·7; H=4·92.

C<sub>15</sub>H<sub>15</sub>O<sub>4</sub>NS requires C=59·0; H=4·9 per cent.

In conclusion, the authors wish to express their indebtedness to the Research Fund Committee of the Chemical Society for the grant which has enabled them to carry out this research.

THE UNIVERSITY,  
MANCHESTER.

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## X.—Isomeric Chromous Chlorides.\*

By WILLIAM ARTHUR KNIGHT and ELIZABETH MARY RICH.

PRUD'HOMME (*Bull. Soc. ind. Mulhouse*, 1889, **59**, 603) stated that chromous chloride was green in hot concentrated acid solution, although its cold dilute solution was blue; hence, from analogy to chromic salts, he assumed the existence of two isomeric forms in solution.

McBain (*Diss.*, Heidelberg) has confirmed this, and succeeded in isolating a solid dark green chromous chloride of unknown degree of hydration, which gave a green solution with water, the solution soon becoming azure-blue.

We have prepared pure chromous chloride by a greatly improved method, and, while confirming the existence of two isomeric chromous chlorides, have further discovered two new solid salts, which are merely lower hydrates of the blue isomeride, one being light green and the other pale blue.

The first part of the present paper deals with the conditions of

\* This paper corresponds with the two abstracts in *Proceedings*, 1910, **26**, 47.

existence of all five hydrates and isomerides. It is shown that the blue isomeride in solution has the formula  $\text{Cl}\cdot\text{Cr}\cdot\text{Cl}_2$ , being highly dissociated into three ions, whilst the green isomeride,  $\text{CrCl}\cdot\text{Cl}_2$ , is well dissociated into two ions.

*The Solid Modifications.*

The blue hydrate,  $\text{CrCl}_2 \cdot 4\text{H}_2\text{O}$ , was prepared by the following modification of Recoura's method \* (*Ann. Chim. Phys.*, 1887, [vi], 10, 10). Chromous acetate is dissolved in concentrated hydrochloric acid in a vacuum,† and the clear solution is boiled down to dryness. If this distillation is too prolonged, or if it is interrupted overnight, the dark green isomeride is usually formed, whilst if the temperature rises above  $51^\circ$  after crystals have begun to appear, the product is pale blue or light green or white, but these are varieties of the blue isomeride, and are finally converted into the stable dark blue hydrate in presence of cold water. The blue crystals are washed by repeated decantation with pure acetone, and the final drying carried out with ether.

Crystals prepared in this way appear to undergo no alteration when left for many months, but, in spite of the high degree of purity of this chromous chloride (especially when it has been reprecipitated from saturated solution by concentrated hydrochloric acid), its solution, on exposure to the air, has a marked disagreeable odour.

The following solid chromous chlorides exist:

Dark blue crystals .....	$\text{CrCl}_2 \cdot 4\text{H}_2\text{O}$
Dark green crystals .....	$\text{CrCl}_2 \cdot 3\text{H}_2\text{O}$
Pale blue crystals .....	$\text{CrCl}_2 \cdot 2\text{H}_2\text{O}$
Light green (amorphous ?) .....	$\text{CrCl}_2 \cdot 2\text{H}_2\text{O}$
White (amorphous ?) .....	$\text{CrCl}_2$

Of these, the first and last were previously known. A direct analysis of the dark green variety was not made, since large quantities could be readily converted into the dry, dark blue modification in a closed flask, and vice versa; consequently, it was proved that the two isomerides are equally hydrated. The analyses of the remaining varieties were carried out by weighing a quantity of the

\* Compare the other methods hitherto employed, which are difficult or laborious: Dammer, *Handb. d. anorg. Chem.*, Bd. III., 1893, 526; Koppel, *Zeitsch. anorg. Chem.*, 1905, 45, 359; Hitterf, *Zeitsch. physikal. Chem.*, 1898, 25, 729; 1899, 30, 481; Ostwald, *ibid.*, 1900, 35, 38, 204; Brauer, *ibid.*, 1901, 38, 441; Doring, *J. pr. Chem.*, 1902, [ii], 66, 65; 1906, [ii], 73, 392; Moissan, *Ann. Chim. Phys.*, 1882, [v], 25, 401; Loewel, *ibid.*, 40, 42; Mazzucelli, *Gazzetta*, 1905, 35, i, 417; Böhringer & Söhne, D.R.-P. 115463.

† If all rubber connexions are well smeared with glycerol, a vacuum may be readily maintained for several months, if necessary.

dark blue crystalline modification in an evacuated flask of known weight, and then converting it into dry specimens of the various lower hydrates by distilling at constant temperature into an evacuated tube containing phosphoric oxide and weighing again. As a check, the lower hydrates in each case were reconverted into the dark blue crystals of the tetrahydrate, which were weighed once more. The transference in a vacuum of the crystals of the dark blue hydrate from one vessel to another was effected by shaking them through the connecting tubes, either with or without acetone.

Conclusive evidence was obtained that water, and not hydrogen chloride, was evolved from the hydrates, even on heating to 180° in a vacuum. This was established by direct analysis (both for chromium and chlorine) of the product obtained after one and the same specimen had been converted into all the modifications in succession.

*The Pale Blue Crystalline Trihydrate*,  $\text{CrCl}_2 \cdot 3\text{H}_2\text{O}$ .—This was prepared by distilling off water from the tetrahydrate at about 50°. This gives a mixture of pale blue trihydrate and light green dihydrate,  $\text{CrCl}_2 \cdot 2\text{H}_2\text{O}$ , but when water is added, the light green portion turns at once into the pale blue. The flask is then heated to 51°, and the pale blue modification which results is quickly dried at the ordinary temperature by evacuation through a phosphoric oxide tube. The only impurity present in the first specimen analysed below was a small amount of the dark blue tetrahydrate, and in the second, very small amounts of both the dark blue and the white modifications:

(I) 12·405 lost 0·993.  $\text{H}_2\text{O} = 8\cdot00$ . (II) 33·823 lost 3·220.  $\text{H}_2\text{O} = 9\cdot52$ .

$\text{CrCl}_2 \cdot 4\text{H}_2\text{O}$  requires loss of  $1\text{H}_2\text{O} = 9\cdot23$  per cent.

*The Light Green Dihydrate*,  $\text{CrCl}_2 \cdot 2\text{H}_2\text{O}$ .—When water was pumped off from crystals of the tetrahydrate at a temperature between 70° and 80°, this dihydrate resulted, and further evacuation at 100° had no effect; the only impurity was a small amount of the anhydrous, white chromous chloride,  $\text{CrCl}_2$ :

(I) 22·354 lost 4·165.  $\text{H}_2\text{O} = 18\cdot63$ . (II) 11·995 lost 2·383.  $\text{H}_2\text{O} = 19\cdot86$ . (III) 12·654 lost 2·391.  $\text{H}_2\text{O} = 18\cdot89$ .

$\text{CrCl}_2 \cdot 4\text{H}_2\text{O}$  requires loss of  $2\text{H}_2\text{O} = 18\cdot48$  per cent.

*Anhydrous White Chromous Chloride*,  $\text{CrCl}_2$ .—This was prepared from the tetrahydrate by exposing the crystals to a temperature of 180° in a vacuum. After determining the loss of water, gravimetric analyses of the chlorine present in the second specimen were carried out; the results gave  $\text{Cl} = 55\cdot2$  and  $55\cdot6$ , whilst  $\text{CrCl}_2$  requires  $\text{Cl} = 57\cdot6$  per cent., showing that very little hydrogen chloride had escaped:

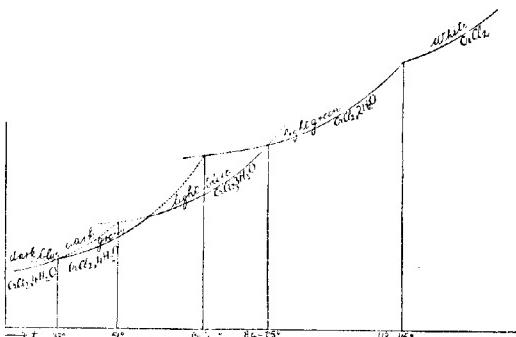
(I). 22·354 lost 8·340.  $H_2O = 37\cdot31$ . (II) 12·654 lost 4·512.  $H_2O = 35\cdot89$ .

$CrCl_2 \cdot 4H_2O$  requires loss of  $4H_2O = 36\cdot96$  per cent.

With regard to the conditions of existence of the various modifications described above, the following relationships were established by direct qualitative observation:

A. *In the Presence of Solution*.—The dark blue  $CrCl_2 \cdot 4H_2O$  is the stable modification up to a temperature of  $38^\circ$ ; it then passes into the dark green  $CrCl_2 \cdot 4H_2O$ , but if the dark green hydrate does not appear, the dark blue modification is stable up to  $51^\circ$ , at which temperature it is replaced by pale blue  $CrCl_2 \cdot 3H_2O$ . The dark green tetrahydrate is stable between  $38^\circ$  and  $60\text{--}70^\circ$ , and then turns into the light green dihydrate  $CrCl_2 \cdot 2H_2O$ . The pale blue trihydrate  $CrCl_2 \cdot 3H_2O$  is converted into light green dihydrate  $CrCl_2 \cdot 2H_2O$  at

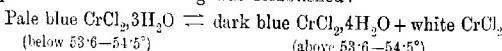
FIG. 1.



$84\text{--}85^\circ$ , and this in turn becomes white anhydrous chromous chloride  $CrCl_2$  at  $113\text{--}115^\circ$ .

The accompanying diagram exhibits these relationships, and represents any property (for example, concentration) of the saturated solutions plotted against the temperature. The observed regions of metastable equilibria are represented by dotted parts of the curves.

B. *Under the Vapour Tensions of the Hydrates Themselves*.—The phase rule demands three simultaneous phases at every equilibrium temperature. The following was established:



(above  $53\cdot6\text{--}54\cdot5^\circ$ )

The dark blue tetrahydrate is recognised at once by its indigo surface colour. The pale blue trihydrate is not instantaneously converted into dark blue tetrahydrate by water; the boundary line

moves at the rate of 2 cm. per hour at 17° in a caked mass of wet crystals which are passing into dark blue crystalline tetrahydrate.

*The Isomerides in Solution.*

The solution is green when hot, concentrated, and acid; blue when cold or dilute. The colour change requires only a few seconds in neutral solution, even at the ordinary temperature, but the presence of acid reduces this velocity enormously, so that the colour change may require weeks for completion. The dark green  $\text{CrCl}_2 \cdot 4\text{H}_2\text{O}$  dissolves to give a green solution; the others produce a blue solution at once.

The two alternative explanations of the structural difference, which has thus been shown to be independent of the state (solid or solution), are the following:

(a) Partial hydrolysis, with the formation of  $\text{CrOH}^+$  as a green cation.

(b) Partial dissociation, forming a green complex ion  $\text{CrCl}^+$  incapable of further dissociation.

Hypothesis (a) is irreconcilable with the fact mentioned by Prud'homme, and confirmed by ourselves, that concentrated hydrochloric acid favours the formation of the green colour; (b) requires that the addition of another chloride would favour the green colour. This was the case when large quantities of potassium chloride were added to a hot solution. This consequently appears to be the most probable explanation, and is analogous to corresponding cases in the chromic salts.

*Determination of Vapour Tension.*

The tensimeter measurements were carried out in an apparatus of the usual type (with several joints inserted in the bulbs to prevent dislodgement of the chromous chloride powder). Mercury was used as manometer liquid, and the height of this was read on a standard glass scale by a telescope fitted with a micrometer eyepiece. The other bulb contained concentrated sulphuric acid, or was simply evacuated by means of a Toepler pump. The following are the final results obtained after an extended series of measurements.

*Experiment I.*

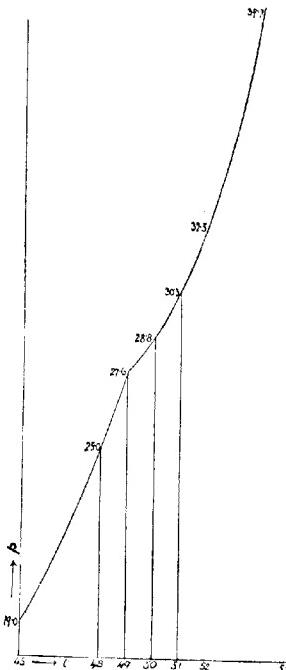
Pale blue  $\text{CrCl}_2 \cdot 3\text{H}_2\text{O}$  + saturated solution (above 49°).

Dark blue  $\text{CrCl}_2 \cdot 4\text{H}_2\text{O}$  + pale blue  $\text{CrCl}_2 \cdot 3\text{H}_2\text{O}$  (below 49°).

Temp.	Pressure, mm.	Temp.	Pressure, mm.
25°	2.9	51°	30.3
35	8.0	52	32.5
45	19.0	55	39.7
48	25.0	60	56.0
49	27.6	65	78.4
50	28.3		

The results obtained between  $45^{\circ}$  and  $55^{\circ}$  are plotted in the accompanying figure, in order to show the very distinct break in the curve at  $49^{\circ}$ , where the dark blue, crystalline tetrahydrate decomposes into pale blue crystals and saturated solution of the trihydrate. Hence the transition temperature is  $49^{\circ}$ , in  $^{\circ}\text{C}$ .

FIG. 2.



agreement with the value  $51^{\circ}$  found by direct observation in the preceding part of the paper.

#### Experiment II.

Light green  $\text{CrCl}_2 \cdot 2\text{H}_2\text{O}$  + saturated solution (above  $84-85^{\circ}$ ).  
Pale blue  $\text{CrCl}_2 \cdot 3\text{H}_2\text{O}$  + light green  $\text{CrCl}_2 \cdot 2\text{H}_2\text{O}$  (below  $84-85^{\circ}$ ).

Temp.	Pressure, mm.	Temp.	Pressure, mm.
12.5°	0.08	75.0°	147.7
50.0	28.5	76.0	150.1
60.2	56.4	77.0	163.1
65.0	79.3	79.5	182.3
70.0	108.0		

If these vapour tensions are plotted, it is seen that the curve is quite smooth up to the highest temperature, thus showing that the transition point, where only  $\text{CrCl}_2 \cdot 2\text{H}_2\text{O}$  in contact with its saturated solution would remain, must lie still higher; according to the data given on p. 90, this transition point lies between  $84^\circ$  and  $85^\circ$ .

These results were confirmed by dilatometer measurements, starting with crystals of the blue tetrahydrate and its saturated solution, and using paraffin oil as dilatometer liquid:

Time at constant temperature.			Time at constant temperature.		
Temp.	Min.	Height.	Temp.	Min.	Height.
86·4	30	56·00	81·1	5	48·00
85·1	25	54·38			
84·0	15	53·05	81·1	10	47·10
84·0	20	53·20			
79·0	5	46·98	81·1	15	46·61
79·0	10	44·45			
79·0	20	41·50	81·1	25	45·55
79·0	30	41·12			
80·0	5	42·78	81·1	30	45·02
80·0	15	42·71	82·0	5	45·25
80·0	20	42·60	82·0	15	45·20
			82·0	25	45·18

From the above experiment, it is evident that the transition point, above which pale blue trihydrate  $\text{CrCl}_2 \cdot 3\text{H}_2\text{O}$  turns into light green dihydrate  $\text{CrCl}_2 \cdot 2\text{H}_2\text{O}$  in contact with saturated solution, is  $82$ — $84^\circ$ , in agreement with the value  $84$ — $85^\circ$  obtained by direct observation. No further determinations with tensimeter or dilatometer were undertaken, as the present confirmations of these two numbers suffice to show the trustworthiness of the other directly observed values.\*

\* The authors are indebted to the kindness of C. W. Spiers of this department for analyses of the specimens which had been used in the tensimeter and dilatometer experiments. These analyses were carried out nine months after the above experiments had been performed, during which time the tensimeter had been untouched, and the substance in the dilatometer bulb had been protected from the atmosphere by the layer of paraffin oil used in the stem as indicating liquid. The contents of the tensimeter were analysed by measuring the volume of oxygen absorbed, followed by gravimetric determination of the whole of the chromium present. The result showed that, after all this time, the crystals in the tensimeter contained 97·95 per cent. of pure chromous chloride.

The analysis of the substance in the dilatometer was carried out both by the method of oxygen absorption and by the reduction of iodine solution, followed in each case by gravimetric determination of the total chromium present. The absorption of oxygen showed that 98·4 per cent. of the chromium was present in the chromous condition, whilst two iodine determinations performed indicated a purity

*Depression of the Freezing Point by the Isomerides in Solution.*

*The Blue Solution.*—The freezing point determinations were carried out in a modification of a Beckmann apparatus, employing a stirrer, in an atmosphere of hydrogen at barometric pressure. The concentration of the solution was determined after the experiment by a gravimetric determination of the chlorine:

Concentration (g.-mol. in 1000 g. H <sub>2</sub> O).	Lowering.	Dissociation per cent.
0·1996	1·050°	93
0·1037	0·526	87

The apparent increase in dissociation in the stronger solution is usual where the lowering is so great.\*

*The Green Solution.*—All attempts to prepare a specimen of the dark green CrCl<sub>3</sub>.4H<sub>2</sub>O previously described proved unavailing; hence, in order to obtain the green solution of chromous chloride, a small quantity of the dark blue tetrahydrate was heated for three days to 95° with a quantity of water just insufficient to dissolve it, to which a few drops of concentrated hydrochloric acid had been added. The arrangements for determining the freezing point were exactly the same as in the case of the blue solution, but the solution was prepared by adding N/10-hydrochloric acid in this case. The freezing point of this dilute green solution having been determined, the solution was analysed (1) for chromium and (2) for chlorine. From the results of the analyses, the amount of hydrochloric acid in the solution was calculated; a hydrochloric acid solution of this strength was then made, and its freezing point determined. The difference between the two freezing points gave the lowering due to the chromous chloride in the solution:

Concentration (g.-mol. in 1000 g. of water).		Lowering caused by CrCl <sub>2</sub> .	Dissociation per cent.
CrCl <sub>2</sub>	HCl.		
0·1090	0·1183	0·771*	73
0·0182	0·1441	0·083	72

The agreement between these two sets of experiments is fortuitous, since it is certain from the method of preparation that the solutions of 104·4 and 95·5 per cent. respectively. Gravimetric determination was rather difficult here on account of the presence of the dilatometer oil.

It is obvious that in any case the presence of even appreciable amounts of the excessively soluble chromic salts, CrCl<sub>3</sub> or CrOHCl<sub>2</sub>, in solution could have no possible influence on dilatometric determinations, since such depend solely on the abrupt alteration in volume of the solid present.

\* Out of 22 cases of halogen compounds of bi- and ter-valent metals, for which data are given in Laudolt-Börnstein's tables, 20 behave as thus mentioned.

contained blue chromous chloride in addition to the green isomeride. The dissociation is calculated, as in the preceding table, assuming the formula  $\text{CrCl}_2$  (dissociating into three ions). It is obvious that the green solution is much less dissociated than the blue isomeride, although markedly so. This result agrees with the formula  $\text{CrCl}\cdot\text{Cl}$ , which represents the green isomeride as dissociating into two ions.

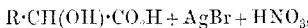
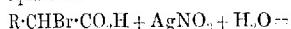
Our thanks are due to Dr. J. W. McBain, at whose suggestion this work was undertaken, for the continued interest he took in it.

THE CHEMICAL DEPARTMENT,  
THE UNIVERSITY, BRISTOL.

*XI.—Reactivity of the Halogens in Organic Compounds. Part V. Interaction of Esters of the Bromo-substituted Fatty Acids with Silver Nitrate in Alcoholic Solution.*

By GEORGE SENTER.

In a previous paper (Trans., 1910, 97, 346) the results of an experimental investigation of the rate of interaction of silver salts with the lower members of the bromo-substituted fatty acids and their sodium salts in aqueous solution have been communicated. In the case of the acids, the reaction is represented by the general equation:



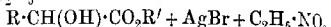
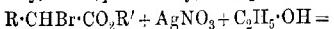
where R represents hydrogen or an alkyl group. It was shown that the rate of reaction increases very considerably with increasing complexity of the group R, and, further, that the reactions are markedly accelerated by silver bromide.

The present communication is mainly concerned with the kinetics of the reactions between silver nitrate and the methyl and ethyl esters of  $\alpha$ -bromoaetic,  $\alpha$ -bromopropionic,  $\alpha$ -bromobutyric,  $\alpha$ -bromo-*isobutyric*, and  $\alpha$ -bromo-*isovaleric* acids in ethyl alcohol, and in some cases in methyl alcohol. It might be anticipated that reactions of this type would proceed according to the equation:



It was found, however, that the amount of nitric acid formed is not equivalent to the silver nitrate used up—with ethyl bromo-

propionate only 50 per cent. of the silver nitrate reappears as nitric acid—and a second reaction must therefore be taking place. This may, in all probability, be represented as follows:



and the total change is therefore rather complicated. The evidence for the view that two simultaneous reactions occur is that the production of nitric acid formed to silver nitrate used up remains constant throughout the reaction within the limits of experimental error (p. 99).

In striking contrast to the behaviour of the free acids in aqueous solution (*loc. cit.*), the rate of reaction with the esters diminishes regularly with increasing complexity of the alkyl group R. On the other hand, the substitution of a methyl group for hydrogen in the ester group R' tends to accelerate the change. A few measurements have also been made in mixtures of alcohol and water, and the effect of indifferent substances, such as acetone, chloroform, and glycerol, on the rate of reaction has been investigated. Under comparable conditions, the reactions are rather more rapid in methyl than in ethyl alcohol.

#### *Units and Method of Measurement.*

The ethyl alcohol used in the experiments was dehydrated by boiling for some days with freshly ignited lime, and finally with metallic calcium. Traces of reducing substances (aldehydes) were removed by distilling the alcohol from dry silver nitrate. Density determinations showed that the alcohol thus prepared was entirely free from water. The methyl alcohol was obtained from Kahlbaum, and was dehydrated by the method used for ethyl alcohol.

The esters were obtained from Kahlbaum, and were tested as regards purity. The esters of bromoacetic and bromopropionic acids were found to be pure; those derived from the higher acids were subjected to fractional distillation, and portions boiling at constant temperature used in the experiments.

The measurements were carried out as described in the previous paper. The solutions were warmed separately in the thermostat, and then mixed in a number of small tubes. In all cases the volume of reaction mixture in each tube measured 12 c.c. At definite times the contents of a tube were transferred to a beaker containing a slight excess of *N*/50-ammonium thiocyanate, and the excess of thiocyanate then estimated by means of *N*/50-silver nitrate.

Unless otherwise stated, the velocity coefficients are calculated by means of the equation for a bimolecular reaction, which, for

equivalent quantities, has the form  $kt = x/a(a-x)$ , where the symbols have the usual significance. In the above equation,  $a-x$  represents the number of c.c. of  $N/50$  thiocyanate equivalent to the amount of silver nitrate in 12 c.c. of the reaction mixture. The velocity coefficients in the tables refer therefore to a concentration of  $1/12 \times 50$  mols. per litre, and, if it is required to refer them to a concentration of 1 mol. per litre, they must be multiplied by 600. The unit of time is one minute throughout. The majority of the experiments were made at  $49\text{--}9^\circ$ ; a few at  $26\text{--}0^\circ$ .

*The Esters in Ethyl Alcohol as Solvent.*

Two or three entirely independent series of measurements were made with each ester, the results being very concordant. Only a few typical results are recorded in the accompanying tables.

TABLE I.

Temperature  $49\text{--}9^\circ$ .

Methyl bromoacetate, $N/10$ . Silver nitrate, $N/20 \times 0.99$ .			Ethyl bromoacetate, $N/10$ . Silver nitrate, $N/20 \times 0.99$ .		
$t$ (min.).	$a - x$ .	$k \times 10^4$ .	$t$ (min.).	$a - x$ .	$k \times 10^4$ .
0	29.6	—	0	29.6	—
60	27.7	0.190	60	27.5	0.208
180	24.2	0.196	180	23.9	0.208
360	20.3	0.192	360	19.7	0.207
1440	8.8	0.180	1440	8.0	0.187
Methyl bromopropionate, $N/10$ . Silver nitrate, $N/20 \times 0.99$ .			Ethyl bromopropionate, $N/10$ . Silver nitrate, $N/20 \times 0.99$ .		
$t$ (min.).	$a - x$ .	$k \times 10^4$ .	$t$ (min.).	$a - x$ .	$k \times 10^4$ .
0	27.85	—	0	27.7	—
180	25.65	0.075	120	26.0	0.092
420	23.20	0.073	360	23.2	0.055
660	21.20	0.073	1200	16.2	0.085
			2520	9.7	0.086
Propyl bromopropionate, $N/10$ . Silver nitrate, $N/20 \times 0.99$ .			Ethyl bromobutyrate, $N/10$ . Silver nitrate, $N/20 \times 0.99$ .		
$t$ (min.).	$a - x$ .	$k \times 10^4$ .	$t$ (min.).	$a - x$ .	$k \times 10^4$ .
0	27.7	—	0	28.45	—
380	23.7	0.087	120	27.65	0.040
1170	16.65	0.087	300	26.60	0.038
2610	9.7	0.085	1280	21.55	0.037
			2820	17.00	0.035
Ethyl bromoisobutyrate, $N/10$ . Silver nitrate, $N/20$ .			Ethyl bromoisovalerate, $N/10$ . Silver nitrate, $N/20 \times 0.99$ .		
$t$ (min.).	$a - x$ .	$k \times 10^4$ .	$t$ (min.).	$a - x$ .	$k \times 10^4$ .
0	28.5	—	0	28.7	—
120	27.3	0.068	180	27.9	0.026
300	25.6	0.062	1140	24.9	0.022
1260	19.3	0.059	2580	22.1	0.019
2700	13.8	0.057			

In examining the above results, it will be noticed that the concentrations of silver nitrate corresponding with  $t=0$  are in some cases considerably less than 30 c.c., which is the value for 12 c.c. of a  $N/20$ -solution of silver nitrate. In these reactions,  $t=0$  is not the time of mixing the solutions, but corresponds with a somewhat later stage of the reaction, in order to eliminate the effect of initial disturbances.

TABLE II.

Temperature 26°.

Methyl bromoacetate, $N/10$	$a-x$ from 29.3 to 25.0	$k \times 10^4 = 0.021$
Silver nitrate, $N/20$	in 1275 minutes.	
Methyl bromopropionate, $N/10$	$a-x$ from 29.3 to 24.2	
Silver nitrate, $N/20$	in 4080 minutes.	$k \times 10^4 = 0.068$

*Methyl Alcohol as Solvent.*

TABLE III.

Temperature 49.9°.

Methyl bromoacetate, $N/10$ .			Ethyl bromobutyrate, $N/10$ .		
Silver nitrate, $N/20$ .			Silver nitrate, $N/20$ .		
<i>t</i> ,	$a-x$ ,	$k \times 10^4$ ,	<i>t</i> ,	$a-x$ ,	$k \times 10^4$ ,
0	26.0	—	0	27.7	—
120	22.35	0.230	120	26.4	0.069
300	18.0	0.230	300	24.65	0.068
1260	7.4	0.217	1380	17.15	0.066
2700	2.3	0.217	2820	11.70	0.062

*Solvent: 95 per cent. Alcohol by Volume.*

TABLE IV.

Methyl bromopropionate,  $N/10$ . Silver nitrate,  $N/20$ .

Temperature 26°.

Temperature 26°.			Temperature 49.9°.		
<i>t</i> ,	$a-x$ ,	$k \times 10^4$ ,	<i>t</i> ,	$a-x$ ,	$k \times 10^4$ ,
0	27.8	—	0	29.5	—
120	25.6	0.083	1200	27.45	0.0096
420	23.1	0.079	2640	25.6	0.0093
600	20.8	0.080	4080	23.9	0.0093

*Solvent: 50 per cent. Alcohol by Volume.*

TABLE V.

Methyl bromoacetate,  $N/10$ .  
Silver nitrate,  $N/20$ .

Temperature 26°.

<i>t</i> (min.).	$a-x$ ,	$k \times 10^4$ ,	Temperature 49.9°.		
			<i>t</i> (min.).	$a-x$ ,	$k \times 10^4$ ,
0	29.5	—	0	29.6	—
120	27.8	0.0109	120	27.5	0.103
2640	24.8	0.0114	360	24.2	0.097

*Ethyl Alcohol with 50 per cent. Acetone, Chloroform, and Glycerol respectively as Solvents.*

TABLE VI.

Ethyl bromoacetate, N/10. Silver nitrate, N/20. Temperature 49·9°.

Solvent.	100 per cent. alcohol.	50 per cent. acetone.	50 per cent. chloroform.	50 per cent. glycerol.
Change of $a - x$	29·6 - 8·0 $\times 10^3$ 0·208 - 0·197	29·9 - 17·6 0·200 - 0·166	29·9 - 20·5 0·148 - 0·115	29·9 - 18·1 0·061 - 0·048

Finally, the results of a series of experiments designed to find what proportion of the silver nitrate appears in the products as nitric acid is given in the accompanying table. A number of tubes containing ethyl bromopropionate and silver nitrate in absolute alcohol were placed in the same thermostat, and simultaneous titrations of the silver nitrate with thiocyanate and of the nitric acid with N/20-sodium hydroxide, using phenolphthalein as indicator, were made. The results, referred to the same standard of concentration, are as follows:

TABLE VII.

$t$ (min.)	$\text{AgNO}_3$ used up.	$\text{HNO}_3$ formed.	Ratio $\text{HNO}_3/\text{AgNO}_3$ .
0	0·0	0·0	—
120	1·8	0·9	50 per cent.
360	4·5	2·3	51 "
660	7·3	3·6	49 "
1440	15·2	7·5	49 "

The figures show that within the limits of experimental error 50 per cent. of the silver nitrate is changed to nitric acid, and the ratio remains constant throughout the reaction. It should be stated that owing to the presence of precipitated silver bromide, the endpoint in titrating nitric acid with sodium hydroxide is not quite sharp, and a correction had to be applied.

*Summary and Discussion of Results.*

(1) *General Character of the Reactions.*—The data quoted in tables I—VII show that the reactions are represented fairly satisfactorily by an equation of the second order, although there is a slight tendency for the velocity-coefficients to diminish as the reactions proceed. In contrast to the behaviour of the acids (*loc. cit.*), the nitric acid formed has only a slight retarding effect, and the catalytic action of the precipitated silver bromide, which is so pronounced in aqueous solution, is also relatively unimportant in alcoholic solution.

The effect of changing the solvent presents several interesting

features. The ratio of the velocity-coefficients for methyl bromopropionate in 100 per cent., in 95 per cent., and in 50 per cent. ethyl alcohol (with water) is 73: 93: 37 (the last figure is not given in the tables), so that the addition of a little water accelerates the reaction, whilst a greater proportion retards it. A similar observation was made by Miss Burke and Donnan (*Zeitsch. physikal. Chem.*, 1909, **69**, 163) for the reaction between silver nitrate and methyl iodide, but so far no plausible explanation of this behaviour has been suggested. It will be observed that in the mixtures with 50 per cent. alcohol, there is a tendency for the coefficients to increase during the reaction. This is doubtless due to partial hydrolysis of the ester in the presence of nitric acid; free bromoacetic acid reacts with silver nitrate rather more rapidly than the corresponding ester (table VIII).

The ratio of the initial velocity-coefficients with ethyl bromoacetate in 100 per cent. alcohol and in mixtures with 50 per cent. of acetone, chloroform, and glycerol respectively is 208: 200: 148: 61 (table VI). This is also the order of increasing viscosities of the solvents, and it is probable that this is the chief factor concerned.

In all cases, the reactions were found to proceed faster in methyl than in ethyl alcohol (tables I and III). For methyl bromoacetate, the ratio is only 1·15: 1, but for ethyl bromobutyrate is about 1·8: 1. Burke and Donnan obtained similar results with the alkyl halogen compounds and silver nitrate, but express no opinion as to the reasons for this behaviour. It is probably also mainly a viscosity effect, the ratio of the viscosities of methyl and ethyl alcohol at 50° being about 1: 1·7.

(2) *Effect of Temperature of Reaction Velocities.*—From a comparison of the data in tables I and II, it is clear that an elevation of temperature from 26° to 49·9° increases the rate of reaction for both methyl bromoacetate and methyl bromopropionate about nine times, so that the temperature-coefficient for 10° is about 2·5. The same value is obtained for methyl bromopropionate in 95 per cent. alcohol.

(3) *Comparison of the Reactivity of Acids and Esters.*—In a previous paper (*loc. cit.*) the rate of reaction of the lower bromo-substituted fatty acids with silver nitrate in aqueous solution has been measured. Since then the speed of the same reactions has been measured in ethyl alcohol, and the results will be communicated in a later paper. A complication arises in this case from the fact that the nitric acid formed in the course of the reaction exerts a very considerable retarding action, much more pronounced even than in aqueous solution (Senter, *loc. cit.*, p. 351), and it is therefore difficult to give a satisfactory velocity-coefficient for these reactions.

It is, however, a matter of considerable interest to compare the reactivities of the acids and esters, and this is done in table VIII, where the velocity-coefficients for the acids are those very near the beginning of the reaction, before the nitric acid has accumulated to any great extent in the system. The coefficients in the accompanying table are expressed in the same units as those used in the present paper, and were all determined under corresponding conditions at 26°:

TABLE VIII.

	$\text{CH}_3\text{Br}\cdot\text{CO}_2\text{H}$ .	$\text{CHMeBr}\cdot\text{CO}_2\text{H}$ .	$\text{CHEtBr}\cdot\text{CO}_2\text{H}$ .	
$k \times 10^3$ .....	0·51 [8·0]	18 [324]	—	in ethyl alcohol
$k \times 10^3$ .....	0·55 [8·8]	55 [880]	250 [4000]	in water "
	$\text{CH}_3\text{Br}\cdot\text{CO}_2\text{Me}$ .	$\text{CHMeBr}\cdot\text{CO}_2\text{Me}$ .	$\text{CHEtBr}\cdot\text{CO}_2\text{Me}$ .	
$k \times 10^3$ .....	0·21 [3·3]	0·086 [1·3]	0·066 [1]	in ethyl alcohol "

The numbers in brackets represent the relative rates of the reactions referred to the slowest, that between methyl bromobutyrate and silver nitrate in ethyl alcohol, as unity.

An examination of the table shows the interesting fact that the reactivities of bromoacetic acid and its methyl ester are of the same order in ethyl alcohol, but when bromopropionic acid and its ester are compared, there is seen to be an enormous difference in the speed with which the bromine is displaced. For reasons given in an earlier paper, however, it appears that the reactions of the bromo-substituted fatty acids with silver nitrate are abnormal, and cannot be compared with the corresponding reactions with the esters. For the same reason, it is probable that most of the instances in the literature in which the relative reactivities of acids and esters are regarded merely as showing the effect of substituting a methyl group for a hydrogen atom, are of no value whatever from this point of view.

(4) *Relative Reactivities of the Esters in Ethyl Alcohol.*—The relative activities of the esters, as expressed by the velocity-coefficients of the reactions with silver nitrate under corresponding conditions (table I), are summarised in table IX:

TABLE IX.

Ester.	$k \times 10^4$ .
Ethyl bromoacetate.....	0·208
" " $\alpha$ -bromopropionate .....	0·085
" " $\alpha$ -bromo- $\beta$ -butyrate .....	0·062
" " $\alpha$ -bromobutyrate .....	0·038
" " $\alpha$ -bromoisovalerate .....	0·022
Methyl bromopropionate.....	0·077
Ethyl " .....	0·085
$n$ -Propyl " .....	0·087

These results may be summed up in the statement that, in a compound of the type  $R\cdot CHBr\cdot CO_2R'$ , the successive displacement of hydrogen in the group R by methyl groups lessens the reactivity of the bromine towards silver nitrate, but, as regards the group  $R'$ , the ethyl ester is rather more reactive than the methyl ester, while the reactivity of the ethyl and propyl esters is the same. It is of interest to note that this order of reactivity of the ethyl esters of bromo-substituted acids exactly corresponds with that found by Reicher (*Annalen*, 1885, **228**, 257) for the saponification of the ethyl esters of the acids themselves by sodium hydroxide. This agreement even extends to the relative reactivity of the butyric and *isobutyric* esters, although ethyl butyrate is saponified only a very little less rapidly than ethyl *isobutyrate*. Slator and Twiss (Trans., 1909, **96**, 93) find that the reactivity of the bromo-substituted esters, measured with regard to sodium thiosulphate, is the same as that given in the present paper, with the exception that ethyl  $\alpha$ -bromo-butyrate is considerably more reactive than the corresponding *iso*-butyrate.

It appears justifiable to ascribe the relative reactivity in the above instances mainly to steric hindrance. The strength of the linking between bromine and the rest of the molecule is doubtless affected to some extent by substitution, but this influence is probably negligible in comparison with the steric effect.

As regards the effect of substitution in the group attached to the oxygen, Slator and Twiss (*loc. cit.*) and Clarke (Trans., 1910, **97**, 416) also find by different methods that the bromine in ethyl bromoacetate is more reactive than that in methyl bromoacetate. As the magnitude of the effect is not greatly beyond the limits of possible experimental error, the possibility was taken into account that the methyl ester might have been converted into the ethyl ester under the influence of the ethyl alcohol used as solvent (compare Purdie, Trans., 1885, **47**, 862; 1887, **51**, 627; 1888, **53**, 391), but the facts (1) that the ratio of the velocities for the two esters is independent of the time during which they remain dissolved in the alcohol before the reaction, and (2) that the ratio of the velocity-coefficients remains constant during the reaction, appear completely to dispose of this suggestion.

Further, it has to be remembered, in connexion with the relative magnitude of the effect, that ethyl bromoacetate is derived from the methyl compound by substitution in the  $\delta$ -position with regard to the bromine, whereas ethyl bromopropionate is derived from ethyl bromoacetate by substitution in the  $\beta$ -position. The observations appear to be accounted for most satisfactorily on the basis of the views as to the effect of substituents on the degree

of affinity developed by Flürsheim (*J. pr. Chem.*, 1905, [ii], **71**, 497; 1907, **76**, 165, 185).

(5) *Internal Mechanism of the Reactions.*—As the total effect is the sum of two simultaneous reactions, and the matter is therefore rather complicated, there is nothing to be gained by discussing the possible mechanism in detail at the present stage. As the order of reactivity of the esters with two such different substituents as silver nitrate and sodium thiosulphate is substantially the same, it appears probable that the reaction is one of direct substitution, the place of the bromine removed by the silver being instantaneously taken by a hydroxy- or ethoxy-group. Euler (*Ber.*, 1906, **39**, 2726) has suggested that in reactions of this type complex ions, containing silver and halogen, play an important part, but there is no direct evidence in favour of this view, and it does not appear to present any advantage over that of direct substitution.

In conclusion, I desire to express my most sincere thanks to Mr. T. J. Ward, of St. Mary's Hospital Medical School, for valuable assistance in the experimental part of the work, and also to the Research Fund Committee of the Chemical Society for a grant which has defrayed most of the expense of the investigation.

CHEMICAL DEPARTMENT,  
ST. MARY'S HOSPITAL MEDICAL SCHOOL, W.

## XII.—*Studies in the Carbazole Series.*

By CARL GUSTAV SCHWALBE and SALOMON WOLFF.

THE object of this research was to prepare mercaptans of carbazole with the intention of converting them into sulphide dyes. For this purpose we have investigated several possible methods of preparation, but in most cases have found that, instead of obtaining the required mercaptan, the derivatives employed were reconverted into carbazole itself.

In the first place, we endeavoured to prepare carbazole mercaptan from 3-aminocarbazole by means of the diazo-reaction. This compound was diazotised and treated with copper powder and sulphurous acid, and later also with copper thiocyanate paste. We were not successful in isolating a mercaptan from the products of reduction, but obtained instead carbazole itself. We also proved that the latter is formed on boiling a solution of diazotised 3-aminocarbazole,

or by treating such a solution with cuprous chloride, according to Sandmeyer.

Another possible method of preparing such mercaptans, namely, by the reduction of the sulphonyl chlorides, cannot, in the case of carbazole, be applied, since the monosulphonic acids are at present unknown. We have, however, closely examined the reduction products of the di- and tri-sulphonic acids of carbazole, prepared according to Schultz and Hauenstein's method (*J. pr. Chem.*, 1907, [ii], 76, 336), but we have only obtained very small quantities of an impure substance with mercaptan-like properties, although we have varied the experimental conditions in many ways.

It was not improbable that monosulphonic acids of carbazole, on reduction, would behave differently from the disulphonic acids, and we accordingly carried out a great number of different sulphonating experiments, always obtaining, however, disulphonic acids, of which we identified two new isomerides.

Furthermore, if both nuclei in carbazole are symmetrically sulphonated, it might be possible that, on introducing, for example, a nitro-group into one nucleus, the other nucleus would take up a single sulphonic acid group, and only a monosulphonic acid would be obtained. On reduction, diazotisation, and boiling with alcohol, such a nitrocarbazolemonosulphonic acid might be expected to yield a carbazolemonosulphonic acid.

We accordingly sulphonated 3-nitrocarbazole, but did not obtain a monosulphonic acid, so that this method also could not be used.

Carbazole may be synthetically prepared from phenylbenzotriazoles according to Graebe and Ullmann (*Annalen*, 1896, 291, 16), and we have attempted to apply a modification of this synthesis to the preparation of a monosulphonic acid by making use of *o*-nitrodiphenylamine-*p*-sulphonic acid. This should be convertible into the corresponding azimino-compound, and the latter into a carbazolemonosulphonic acid. We succeeded, in fact, in preparing 1-phenyl-1: 2: 3-benzotriazole-5-sulphonic acid, but, on heating it, obtained carbazole itself instead of the expected monosulphonic acid. It would therefore seem that at the high temperature of formation the monosulphonic acid of carbazole decomposes, with formation of carbazole. In further support of this, we have shown that on heating the salts of the disulphonic acids of carbazole at a high temperature, carbazole is regenerated. Schultz and Hauenstein have also proved that the potassium salt of a disulphonic acid of carbazole, on being heated with potassium cyanide, gave rise to carbazole. From these data it seems clear that certain of the carbazole derivatives show in their reactions a strong tendency to regenerate carbazole, and that the ordinary transformations

which occur readily in the benzene series do not here take place.

### EXPERIMENTAL.

#### *3-Aminocarbazole.*

Ruff and Stein (*Ber.*, 1901, **34**, 1677) obtained 3-aminocarbazole on reducing nitronitrosocarbazole with stannous chloride and hydrochloric acid. We modified this method by using technical sodium sulphide. Nitronitrosocarbazole is mixed with 10 parts of 96 per cent. alcohol, and to this mixture 10 parts of concentrated sodium sulphide solution are added. A deep red coloration is produced, and the mixture has an ammoniacal odour. The product is heated on the water-bath until a sample of the mixture no longer gives a red colour with aqueous sodium sulphide. As intermediate product, a substance, melting at 210°, was isolated, which was probably identical with nitrocarbazole. The methods described in D.R.P. 122852 and 134983, and also that recommended by Ziersch (*Ber.*, 1909, **42**, 3797), namely, reduction with sodium hyposulphite, led, in our experiments, to less pure products.

#### *Carbazoledisulphonic Acids.*

Schultz and Hauenstein heated carbazole with the quantity of concentrated sulphuric acid necessary for the formation of a monosulphonic acid, at a temperature of from 70° to 75° during six to seven hours. After conversion into the barium salt, these authors obtained a separation of crystals only after the concentrated solution had been kept for a long time, but the barium salt prepared by us crystallised out directly on cooling the solution, as a voluminous, colourless mass. On reconverting this barium salt into the potassium salt, and treating the latter with phosphorus pentachloride, a *disulphonyl chloride* was obtained, which crystallised from acetone in colourless leaflets, and gave, with ammonia, unlike Schultz and Hauenstein's product, a *disulphonamide*, having no definite melting point.

When heated under pressure with 48 per cent. sulphuric acid at 120°, or with water at 130°, the potassium salt of this acid gives rise to carbazole.

The *disulphonyl chloride* gave on analysis:

0·1488 gave 0·123 AgCl. Cl=20·45.

0·1668 " 0·2058 BaSO<sub>4</sub>. S=16·92.

C<sub>13</sub>H<sub>7</sub>O<sub>4</sub>NCl<sub>2</sub>S<sub>2</sub> requires Cl=19·50; S=17·58 per cent. •

Analysis of the *disulphonamide* furnished the following numbers

0·175 gave 0·2518 BaSO<sub>4</sub>. S=19·76.

0·148 „ 16·5 c.c. N<sub>2</sub> at 21° and 750 mm. N=12·97.

C<sub>12</sub>H<sub>11</sub>O<sub>4</sub>N<sub>3</sub>S<sub>2</sub> requires S=19·69; N=12·92 per cent.

Carbazole is readily sulphonated on treatment with mono potassium disulphate, KH<sub>3</sub>(SO<sub>4</sub>)<sub>2</sub>, at about 100°. The potassium salt of the sulphonic acid formed proved to be a mixture of di- and tri-sulphonic acids.

We have also found that carbazole is easily sulphonated by 67 per cent. sulphuric acid.

Ten grams of carbazole are heated with 50 c.c. of 67 per cent sulphuric acid at 115° for some hours, the mixture being stirred. By this process a fairly soluble barium salt and a crystalline potassium salt of *carbazoledisulphonic acid* are produced. The *disulphonyl chloride* melts at 102°, reacts in the cold with ammonia giving a yellow coloration, and finally dissolves, but a disulphonamide could not be obtained.

On heating the potassium salt with 48 per cent. sulphuric acid or with water under pressure, it remains unaltered, and in this respect also differs from the above-described disulphonic acid, which regenerates carbazole.

On analysis of the *potassium salt*:

0·1500 gave 0·1628 BaSO<sub>4</sub>. S=15·20.

0·1500 „ 0·1630 BaSO<sub>4</sub>. S=15·21.

C<sub>12</sub>H<sub>7</sub>O<sub>6</sub>NS<sub>2</sub>K<sub>2</sub> requires S=15·88 per cent.

The *disulphonyl chloride* was also analysed:

0·1520 gave 0·1218 AgCl. Cl=19·83.

0·1520 „ 0·1214 AgCl. Cl=19·76.

C<sub>12</sub>H<sub>7</sub>O<sub>6</sub>NCl<sub>2</sub>S<sub>2</sub> requires Cl=19·50 per cent.

Thus the existence of at least two isomeric disulphonic acids is shown by these experiments. The difference in properties exhibited by the acid prepared by us by Schultz and Hauenstein's method cannot as yet be satisfactorily explained.

#### *Sulphonation of 3-Nitrocarbazole.*

Five grams of 3-nitrocarbazole were heated with 25 c.c. of 67 per cent. sulphuric acid at 130–140° until dissolved. After separation of a tarry by-product, the filtrate was treated with barium carbonate, and a yellow, amorphous barium salt was isolated, which could not be obtained crystalline:

0·928 gave 0·3832 BaSO<sub>4</sub>. Ba=24·30.

0·1554 „ 0·1270 BaSO<sub>4</sub>. S=11·22.

C<sub>12</sub>H<sub>6</sub>O<sub>6</sub>N<sub>2</sub>S<sub>2</sub>Ba requires Ba=26·95; S=12·62 per cent.

These results indicate that a mixture of mono- and di-sulphonic id is formed.

On reducing the nitrocarbazolesulphonic acid by Claisen's method, small quantity of a silver-grey potassium 3-aminocarbazole-di-sulphonate was isolated:

0·1436 gave 8·2 c.c. N<sub>2</sub> at 22° and 747 mm. N=6·4.  
 $C_{12}H_8N_2O_6S_2K_2$  requires N=6·7 per cent.

*1-Phenyl-1: 2: 3-benzotriazole-5-sulphonic Acid.*

This acid was obtained by the diazotisation of *o*-aminodiphenylamine-*p*-sulphonic acid. The latter was prepared by the action of quinoline on *p*-chloro-*m*-nitrobenzenesulphonic acid, and reduction of the *o*-nitrodiphenylaminesulphonic acid formed.

*o*-Aminodiphenylaminesulphonic acid is described in the literature as an indistinctly crystalline solid. We obtained it in well-defined lightly violet needles.

On diazotisation, a red solution was obtained, which did not combine with phenols. On evaporation of this, a brown, amorphous substance separated out, which, on being slightly heated on platinum oil, swells up and leaves a grey, iridescent mass. On slowly heating this triazole at 390–400°, carbazole sublimes on the sides of the vessel:

0·1504 gave 17·8 c.c. N<sub>2</sub> at 15° and 757 mm. N=13·8.  
 0·1504 " 18·4 c.c. N<sub>2</sub>, 15°, 757 mm. N=14·13.  
 0·1488 " 0·1090 BaSO<sub>4</sub>. S=10·6.  
 $C_{12}H_8O_3N_3S$  requires N=15·27; S=11·63 per cent.

INSTITUTE FOR ORGANIC CHEMISTRY,  
 TECHNISCHE HOCHSCHULE, DARMSTADT.

XIII.—*The Absorption Spectra of Some Derivatives and Isomerides of 1: 2-Diketo- $\Delta^3$ -cyclopentene.*

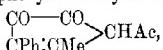
By JOHN EDWARD PURVIS.

THE author has already given an account of an investigation on the absorption spectra of some diketopyrrolone compounds (Trans., 1910, 97, 2535). The results showed that (1) the diketonic structure gives rise to the production of a well-marked colour and absorption; (2) the introduction of a methyl or a propyl group in an aromatic side-chain produces no fundamental change in the colour or the absorption; (3) the introduction of a methoxy- or a methylenedioxy-

group in an aromatic side-chain does not fundamentally alter the colour or the corresponding absorption, but another more refrangible band is produced characteristic of each type of radicle; (4) the replacement of oxygen in a ketonic group by the  $\text{N}\cdot\text{NHPH}$  group produces a change in the colour and the absorption, so that two bands are developed, the less refrangible one being the stronger; (5) the replacement of both oxygen atoms and the establishment of a phenazine ring is marked by a further change in the colour from red to yellow, a decrease in the strength of the less refrangible band, and an increase in the strength of the more refrangible one; (6) the increased weight of the molecule shifts the position of general absorption towards the more refrangible regions.

That there is an intimate connexion between the absorption and the ketonic constitution is further shown from a consideration of the following 1: 2-diketo- $\Delta^3$ -cyclopentene compounds described by Ruhemann and Merriman (Trans., 1905, **87**, 1383) and by Ruhemann (Trans., 1909, **95**, 984, 1603; 1910, **97**, 462, 143). From chemical considerations, the authors ascribed the following constitutional formulae to the various compounds:

1 : 2-Diketo-5-acetyl-3-phenyl-4-methyl- $\Delta^3$ -cyclopentene,



red.

The corresponding oxime,  $\begin{array}{c} \text{C}(\text{NOH})\cdot\text{CO} \\ || \\ \text{CPh}=\text{CMe} \end{array} > \text{CHAc}$ , orange-yellow.

The corresponding phenylhydrazone,  $\begin{array}{c} \text{C}(\text{N}\cdot\text{NHPH})\cdot\text{CO} \\ || \\ \text{CPh}=\text{CMe} \end{array} > \text{CHAc}$ , yellow.

The sodium compound,  $\begin{array}{c} \text{C}(\text{ONa})\cdot\text{CO} \\ || \\ \text{CPh}=\text{CMe} \end{array} > \text{CHAc}$ , blue.

The isophenazine derivative,  $\begin{array}{c} \text{CPh}=\text{C}\cdot\text{NH} \\ || \\ \text{CMe}\cdot\text{C}\text{Ac}\cdot\text{C}=\text{N} \end{array} > \text{C}_6\text{H}_4$ , raspberry-red.

Solutions of these substances in milligram-molecules by weight in cold absolute alcohol have been investigated in the usual way. For example,  $N/100$ -solution means that one milligram-molecule by weight of the substance was dissolved in 100 c.c. of cold absolute alcohol; a  $N/1000$ -solution means that one milligram-molecule by weight of the substance was dissolved in 1000 c.c. of cold absolute alcohol.

The red 1: 2-diketo-5-acetyl-3-phenyl-4-methyl- $\Delta^3$ -cyclopentene in  $N/100$ -alcoholic solution was examined through various thicknesses of the solution, ranging from 3 mm. to 45 mm., but no band was observed. The positions where general absorption began through

The following thicknesses expressed in Ångström's units and in oscillation frequencies were:

		$\lambda$	$\frac{1}{\lambda}$
3 mm. thickness		3350	2696
6 " "		3920	2550
9 " "		5000	1999
12 " "		5320	1879
30 " "		5450	1833
45 " "		5450	1833

The  $N/100$ -solution was then diluted with absolute alcohol, so that 1000 c.c. contained one milligram-molecule by weight, or  $N/1000$ -strength. This solution was examined, and a band became apparent through 2 mm. thickness. The positions where general absorption began through greater thicknesses are also noted in the following table:

2 mm. thickness band between $\lambda$ 3250 and $\lambda$ 2820		$\lambda$	$\frac{1}{\lambda}$
9 "	" general absorption began at	3490	2864
30 "	" "	3830	2609

The  $N/1000$ -alcoholic solution was then diluted with alcohol, so that the solution contained one milligram-molecule in 10,000 c.c. absolute alcohol, and on examining this  $N/10,000$ -solution the band in the ultra-violet was better marked, and the absorption curve has been drawn (Fig. 1, I). The head of the band is at about 3325 (oscillation frequencies).

A  $N/10,000$ -solution of the yellow-coloured oxime of diketoacetyl-phenylmethylcyclopentene was also examined, and it exhibited no band through the following thicknesses. The following numbers give the positions where general absorption began:

2 mm. thickness	$\lambda$	$\frac{1}{\lambda}$
4 " "	2180	4556
10 " "	2270	4103
20 " "	2520	3965
30 " "	2780	3595
	2890	3459

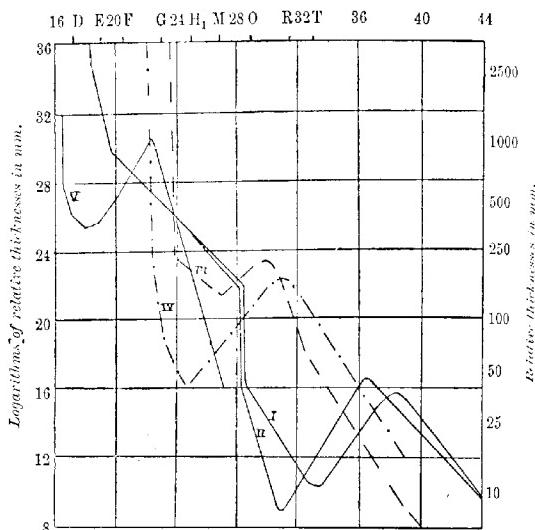
but on examining a  $N/1000$ -solution of the oxime a strong band was exhibited, the absorption curve of which has been drawn, and the head of which is at about 2470 (oscillation frequencies) (Fig. 1, IV).

A  $N/10,000$ -solution of the yellow phenylhydrazone of diketo-phenylmethylacetyl-cyclopentene was also examined, but no band was exhibited through the following thicknesses, and the numbers represent the positions where general absorption began:

	$\lambda$	$\frac{1}{\lambda}$
4 mm. thickness	2380	4199
8 " "	2590	3859
16 " "	2770	3608
24 " "	2850	3506
32 " "	3080	3246

On examining a  $\lambda/1000$ -solution, however, a band was developed, the curve of which has been drawn (Fig. 1, III). The head of the

FIG. 1.

*Oscillation frequencies.*

- I. Alcoholic solution of 1:2-diketo-5-acetyl-3-phenyl-4-methyl- $\Delta^3$ -cyclopentene.
- II. " " the sodium compound of 1:2-diketo-5-acetyl-3-phenyl-4-methyl- $\Delta^3$ -cyclopentene.
- III. " " phenylhydrazone of " " " "
- IV. " " oxime of " " " "
- V. Benzene solution of 5-acetyl-3-phenyl-4-methyl- $\Delta^3$ -cyclopentene.

band is at about 2700 (oscillation frequencies). It may be mentioned here that hydroxylamine hydrochloride shows no bands in the ultra-violet (Hartley and Dobbie, Trans., 1900, 77, 318), and the author has shown that solutions of phenylhydrazine exhibit no bands (Trans., 1910, 97, 2540).

As exhibited from the above numbers, the red colour of the

AND ISOMERIDES OF 1:2-DIKETO- $\Delta^3$ -CYCLOPENTENE. 1:1

1:2-diketocyclopentene compound is produced by a general absorption of the yellow, blue, green, and violet rays well in the visible spectrum, and only in the  $N/10,000$ -solution is there a band apparent in the ultra-violet regions. In the red diketonic pyrroline before described (*loc. cit.*), there is a band which is between the regions of the visible and the invisible spectrum. The corresponding  $N/10,000$ -solutions of the oxime and of the phenylhydrazone of the 1:2-diketocyclopentene compound do not show bands through equal thicknesses; but in each case a band is apparent in the less refrangible regions. The band of the heavier phenylhydrazone has greater shift towards the more refrangible regions, and this phenomenon is comparable with similar phenomena observed in the diketopyrrolone derivatives (*loc. cit.*).

The effect of sodium hydroxide on the 1:2-diketocyclopentene compound was shown by Ruhemann (*loc. cit.*) to change the colour from red to blue. In this blue compound, and in the *isophenazine* derivative, Ruhemann suggested that the positional linking of the ring is different from the others, and as indicated in the constitutional formulae on p. 108. On examining and comparing the blue solution produced by adding one drop of sodium hydroxide to the red solution of the 1:2-diketocyclopentene compound, the change in colour was accompanied by the production of a narrower and more persistent band in the ultra-violet, and a greater shift towards the less refrangible regions (Fig. I, II). Its head is at about 3080 (oscillation frequencies). A  $N/100$ -solution of the blue-coloured solution was also examined, but no other band was observed, and the positions where general absorption began through the following thicknesses were:

	$\lambda$	$\frac{1}{\lambda}$
3 mm. thickness	4020	2487
6 " "		
9 " "		
12 " "		
15 " "		
18 " "		

No rays were transmitted,  
for the panchromatic plates  
contained no images of any  
part of the spectrum.

That is to say, the blue colour was produced by a general absorption of the red and yellow rays, accompanied by a narrowing of the band in the ultra-violet.

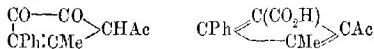
In the *isophenazine* raspberry-red derivative, where both the oxygen atoms in the ketonic groups are replaced, and where Ruhemann suggests a positional change in the valencies of the cyclopentene nucleus, a large band is exhibited in  $N/1000$ -solution in benzene (the substance is insoluble in alcohol). The absorption curve of this band has been drawn (Fig. I, V), and corresponds with the purple colour. Its head is at about 1800 (oscillation

frequencies).  $N/10,000$ -Solutions of the substance were also examined, but no other bands became apparent, and benzene itself through 2 mm. thickness absorbs the light beyond  $\lambda 3010$ . The positions where general absorption began in the  $N/10,000$ -solution in benzene were:

	$\lambda$	$\frac{1}{\lambda}$
2 mm. thickness	3010	3320
10 " "	3290	3038
20 " "	3580	2791
30 " "	3720	2687

It is important to compare the bands of the phenylhydrazone and the isophenazine derivative of the diketocyclopentene with the corresponding derivatives of the diketopyrrolone (*loc. cit.*). In the latter substance there is a second more refrangible band produced which is absent in the former. It follows from this comparison that the absorption is conditioned, not only by the diketonic structure, but also by the type of ring in which the structure occurs. The diketonic structure means the production of a striking colour, and the colour and selective absorption are altered when the oxygen atoms are replaced in the ketonic radicles by oxime and phenylhydrazone radicles. The absorption is also modified in different directions of the spectral regions according to the type of nucleus and the substituted radicles, as well as by alterations in the positional valencies of the atoms of the ring.

Other substances described by Ruhemann and Merriman (*loc. cit.*) have also been examined. The formulæ ascribed to these compounds from chemical considerations are:



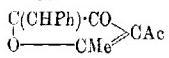
1:2-Diketo-5-acetyl-3-phenyl-4-methyl- $\Delta^3$ -cyclopentene, red.

*A.*

(Described above.)

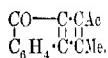
3-Acetyl-1-phenyl-4-methyl-1:3-cyclobutadiene-2-carboxylic acid, colourless.

*B.*



4-Keto-3-acetyl-5-benzylidene-2-methyl-di-hydrofuran, light yellow.

*C.*



Indone - cyclo-methylacetoo-ethylene, reddish brown.

*D.*

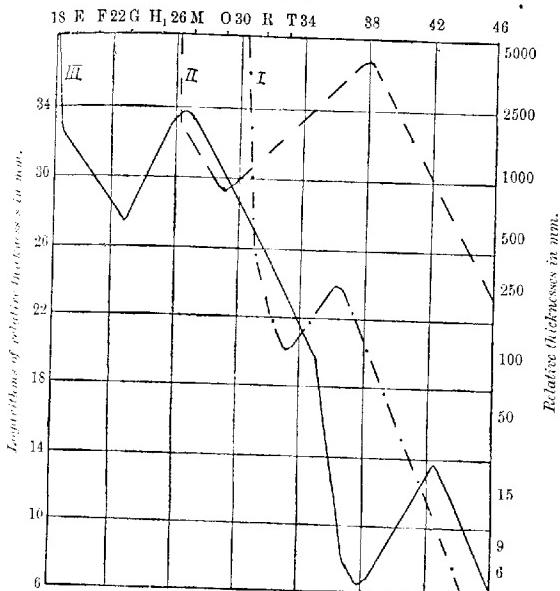
The substances *A*, *B*, and *C* are isomeric compounds. The absorption curve for *A*, the 1:2-diketo- $\Delta^3$ -cyclopentene compound, has been already drawn (Fig. 1, I) and discussed in relation to its derivatives.

— The colourless substance *B*, 3-acetyl-1-phenyl-4-methyl-1:3-cyclo-

butadiene-2-carboxylic acid, which does not possess a ketonic structure, was examined in various strengths of alcoholic solutions, and  $N/1000$ -solution exhibited a weak band in the ultra-violet, the curve of which has been drawn (Fig. 2, I). It is interesting to note that the position of this band, whose head is at 3300, coincides

FIG. 2.

## Oscillation frequencies,



I. Alcoholic solution of 3-acetyl-1-phenyl-4-methyl-1:3-cyclobutadiene-2-carboxylic acid.

II. " " 4-keto-3-acetyl-5-benzylidene-2-methylhydrofuran.

with that found in the 1:2-diketocyclopentene compound itself, and it is possibly a benzenoid band (Fig. 1, I).  $N/100$ -Solutions were also examined, and at 2 mm. thickness the band was observed between  $\lambda$  3140 and  $\lambda$  2820, and the positions where general absorption begins in  $N/100$ -solution of the substance B are:

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2 mm. thickness band between  $\lambda$  3140 and  $\lambda$  2820

			$\frac{1}{\lambda}$
10 "	"	general absorption began	8280      3047
20 "	"	"      "	3320      3104
30 "	"	"      "	3330      3002
40 "	"	"      "	3345      2989
50 "	"	"      "	3350      2983
60 "	"	"      "	3360      2976

$N/10,000$ -Alcoholic solutions of the substance *B* were also examined, but no band was observed, and the positions where general absorption began were:

		$\frac{1}{\lambda}$
2 mm. thickness		2190      4564
10 "	"	2345      4263
20 "	"	2500      3997
30 "	"	2535      3943

The yellow compound *C*, 4-keto-3-acetyl-5-benzylidene-2-methylhydrofuran,  $\alpha$ -ketonic substance, in  $N/10,000$ -solution exhibited a band the curve of which has been drawn (Fig. 2, II). The head of the band is at about 2900, and it is different in position, in intensity, and in persistence from the bands of either *A* or *B*. In  $N/100$ -solution of *C* there was no band, and the positions where general absorption began were:

		$\frac{1}{\lambda}$
2 mm. thickness		2800      2631
10 "	"	3940      2537
20 "	"	4050      2468
30 "	"	4039      2474

In  $N/1000$ -solution of *C* there was the above band observed through 2 mm. thickness, and the positions where general absorption began through greater thicknesses were:

2 mm. thickness band between  $\lambda$  3670 and  $\lambda$  2900

		$\frac{1}{\lambda}$
10 "	"	general absorption begins at      3790      2637
30 "	"	"      "      3650      2739

The reddish-brown substance *D*, indone cyclomethylacetethylene, a ketonic compound to which a double ring formula has been ascribed, exhibits two bands. A  $N/100$ -solution shows a band the head of which is at about  $1/\lambda$  2260 (Fig. 2, III); and a  $N/10,000$ -solution exhibits another band the head of which is at about  $1/\lambda$  3780. It is evident, therefore, that these two bands distinguish it from the substances *A*, *B*, and *C*, in that it has two bands whilst the others have one. The production of the two rings means the production of two absorption bands, the band

at 3780 corresponding with the ring  $C_6H_4 <$ , and the band at 2360 corresponding with the ring  $\begin{array}{c} -C=C- \\ | \quad | \\ C \quad C- \end{array}$ .

The colour of both the compounds *C* and *D*, like that of *A*, are produced by a general absorption of the rays well in the visible spectrum, *A* being red, *C* being light yellow, and *D* being reddish-brown.

#### *General Conclusions.*

It is clear from a comparison of these observations and of those of the 2:3-diketopyrrolines (*loc. cit.*) that (1) the colour is determined primarily by the presence of either a monoketonic or a diketonic structure; (2) the absorption in the more refrangible regions of the monoketonic compounds is further determined by the type of ring in which the ketonic structure occurs; (3) in the 1:2-diketonic *cyclopentene* compounds, the colour is modified in the direction of the more refrangible regions by the introduction of an oximo- or of a  $:N\cdot NHPh$  group, a result precisely analogous to that which has been previously observed in the 2:3-diketopyrrolines; (4) in the 1:2-diketonic *cyclopentene* compounds, the absorption in the ultra-violet of the phenylhydrazone or of the *isophenazine* derivative is wholly different from that of the corresponding substances derived from the 2:3-diketopyrrolines; and (5) the difference in the *isophenazine* compound may be explained partly as the result of an alteration in the positional valencies of the ring, as suggested by Ruhemann (*loc. cit.*). The explanation also applies to the blue sodium compound of the 1:2-diketocyclopentene. In the *isophenazine* compound, the absorption is not moved in the direction of the more refrangible rays like that which occurs in the phenazine obtained from the diketopyrroline. Further, as regards the blue sodium compound of the 1:2-diketocyclopentene, besides the change in colour from red to blue, the band in the ultra-violet becomes narrower and more persistent, and is shifted towards the more refrangible end of the spectrum.

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UNIVERSITY CHEMICAL LABORATORY,  
CAMBRIDGE.



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2454	*19	for "a thousand" read "ten thousand."
2460		last number in 6th column of <i>Viscosities at 0°</i> , for "9703" read "8703," and fourth number of 7th column of <i>Viscosities at 10°</i> , for "5236" read "9236."
2462		Fig. 2, for "Normality" read "Normality."

\* From bottom.



at 3780 corresponding with the ring  $C_6H_4<$ , and the band at 2260 corresponding with the ring  $\begin{array}{c} \text{C:C} \\ \text{---} \\ \text{C:C} \end{array}$ .

The colour of both the compounds *C* and *D*, like that of *A*, are produced by a general absorption of the rays well in the visible spectrum, *A* being red, *C* being light yellow, and *D* being reddish-brown.

#### *General Conclusions.*

It is clear from a comparison of these observations and of those of the 2:3-diketopyrrolines (*loc. cit.*) that (1) the colour is determined primarily by the presence of either a monoketonic or a diketonic structure; (2) the absorption in the more refrangible regions of the monoketonic compounds is further determined by the type of ring in which the ketonic structure occurs; (3) in the 1:2-diketonic cyclopentene compounds, the colour is modified in the direction of the more refrangible regions by the introduction of an oximo- or of a :N:NHPh group, a result precisely analogous to that which has been previously observed in the 2:3-diketopyrrolines; (4) in the 1:2-diketonic cyclopentene compounds, the absorption in the ultra-violet of the phenylhydrazone or of the isophenazine derivative is wholly different from that of the corresponding substances derived from the 2:3-diketopyrrolines; and (5) the difference in the isophenazine compound may be explained partly as the result of an alteration in the positional valencies of the ring, as suggested by Ruhemann (*loc. cit.*). The explanation also applies to the blue sodium compound of the 1:2-diketocyclopentene. In the isophenazine compound, the absorption is not moved in the direction of the more refrangible rays like that which occurs in the phenazine obtained from the diketopyrroline. Further, as regards the blue sodium compound of the 1:2-diketocyclopentene, besides the change in colour from red to blue, the band in the ultra-violet becomes narrower and more persistent, and is shifted towards the more refrangible end of the spectrum.

My thanks are due to the Government Grant Committee of the Royal Society, by whose assistance the spectroscope was purchased, and to Dr. Ruhemann for specimens of the pure substances.

UNIVERSITY CHEMICAL LABORATORY,  
CAMBRIDGE.

XIV.—*Preparation of Ammonium Nitrite by the Sublimation in a Vacuum of a Mixture of Ammonium Chloride and Alkali Nitrites.*

By PAÑCHĀNAN NEOGI, M.A., and BIRENDRA BHUSAN ADHICARY, M.A.

RĀV (Trans., 1909, **95**, 345) has recently shown that solid ammonium nitrite sublimes in small quantities with decomposition when a dilute solution (0·7 to 2·0 per cent.) of the salt, obtained by the double decomposition of silver or barium nitrite and ammonium chloride or sulphate respectively, is gently heated in a vacuum. We have now found that the salt may be obtained in fairly large quantities by evaporating and subliming in a vacuum a very concentrated solution of a mixture of ammonium chloride and sodium or potassium nitrite.

EXPERIMENTAL.

The apparatus employed is as follows. A distilling flask of fairly large capacity is connected with a condenser, to the other end of which are attached two filtering flasks connected with each other by means of pressure tubing, and immersed in cold water. The first serves as a receiver, and the second, which contains a quantity of concentrated sulphuric acid, is connected with a manometer and a Geryk pump. The flask is heated in a water- or, better, paraffin-bath.

Twenty-three grams of ammonium chloride and 35 grams of sodium nitrite (or 42 grams of potassium nitrite) were dissolved in the minimum quantity of cold water, the solution transferred to the distilling flask, the latter connected with a condenser, and the Geryk pump set to work. The flask was immersed in a paraffin-bath up to the portion containing the solution, and the temperature of the bath was maintained between 50° and 60°. Water distilled with gentle frothing, but without bumping. Considerable bumping, however, takes place if a naked flame is used instead of a bath. The filtering flasks dipped in cold water arrested any escaping moisture, which would otherwise enter the pump and condense in the manometer. When a certain concentration was reached, minute bubbles of gas were evolved, and the mercury column descended slightly. The pump was worked from time to time to maintain the vacuum. Special care should be taken at the time when the mass just becomes solid. At this point the temperature should not be raised above 60°, and the pump should be constantly worked, as otherwise the whole of the nitrite would decompose with almost

explosive violence. When once the mass has solidified and become perfectly quiescent, the liability of the nitrite to decompose is almost removed. The temperature of the bath was then gradually raised to 80°, when the solid nitrite began to sublime.\* The flask was gradually lowered into the bath as the sublimate rose higher and higher, until the whole mass was collected as a thick, circular crust at the top of the bulb of the flask. The bath was then removed, and air was admitted, not by opening the screw in the pump (as in that case the moist air would dissolve the whole quantity of the extremely hygroscopic nitrite formed), but by gently opening the cork of the flask. The bottom of the latter was then broken, and the solid mass quickly scraped off with a spatula. The substance was so very deliquescent that it was difficult to remove the whole quantity of the salt obtained. A considerable portion of the salt decomposed, and a part escaped into the condenser with the steam. The liquid collected in the receiver contained much ammonium nitrite as well as a small quantity of the chloride.

The liquid in the receiver was transferred to the distilling flask, and evaporated in a vacuum as before. A second crop of the nitrite sublimed, and was collected.

#### *Analysis.*

The substance obtained consists of fine flakes, and is extremely hygroscopic. It liberates iodine copiously when treated with potassium iodide solution acidified with dilute hydrochloric acid. When silver nitrate solution is added to the solution of the substance, a crystalline precipitate of silver nitrite is obtained, which dissolves in hot water, leaving in some cases a faint opalescence. That the substance does not contain any ammonium nitrate is shown by the fact that the amount of nitrogen yielded by the "urea" method is identical with that of the nitric oxide obtained by the Crum-Frankland method. The "ammonia" nitrogen in the salt, as estimated by the Nessler test, bears the ratio of 1:1 to the nitrogen in the acid radicle. The substance is therefore proved to be pure ammonium nitrite.

The salt may be kept undecomposed in an ordinary desiccator over concentrated sulphuric acid or in sealed tubes. If kept in a vacuum desiccator, the salt vaporises, and within two or three days the greater part is lost, and the odour of nitrous fumes, formed by the action of the sulphuric acid on the vaporised nitrite, is perceived on opening the desiccator.

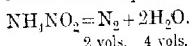
\* It was found by blank experiments that solid ammonium chloride commenced to sublime in small quantities when the temperature of the bath was above 140° and the pressure was between 10 and 20 mm.

Ammonium nitrite volatilises in steam. A solution of the salt was placed in a distilling flask, and steam was admitted into it. The pump was worked, and after some time the distillate was tested, when appreciable quantities of ammonium nitrite were found in it.

We confirm Rây's observation (*loc. cit.*) that the re-sublimed salt does not explode on heating, although, as already pointed out, the salt sometimes decomposes with almost explosive violence as its concentrated solution just becomes solid.

#### *Vapour Density of Ammonium Nitrite.*

The question whether the sublimation of ammonium nitrite is really a case of sublimation or dissociation was left open by Ray (*loc. cit.*). In order to decide the point, we determined the vapour density of the salt according to Hofmann's method. Using chloroform vapour to heat the Hofmann tube, it was found that the solid substance was only partly vaporised, and with ethyl alcohol, also, it was found that some portion of the substance still remained solid. At 100°, using steam, the density of the resulting gas was found to be 12·7. This result shows that at 100° the salt almost entirely decomposes according to the usual equation:



The decomposition according to the above reaction, in which one molecular proportion of ammonium nitrite decomposes into two volumes of nitrogen and four volumes of water vapour, would give the vapour density of ammonium nitrite as 10·6, the density actually obtained being 12·7.

CHEMICAL LABORATORY, RAJSHAHI COLLEGE,  
RAJSHAHI, EASTERN BENGAL, INDIA.

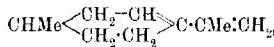
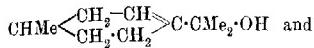
#### XV.—On dl- and d- $\Delta^2$ -m-Menthene(8) and dl- and d- $\Delta^{2:8(9)}$ -m-Menthadiene.

By WALTER NORMAN HAWORTH (1851 Exhibition Scholar of Manchester University), WILLIAM HENRY PERKIN, jun., and OTTO WALLACH.

In a paper published recently (*Trans.*, 1910, **97**, 1427), attention was directed to the difficulty of obtaining substances belonging to the terpene group, and especially the terpenes themselves, in a condition pure enough to allow of the accurate determination of their physical

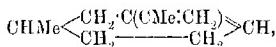
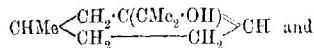
properties. In order that such substances may be characterised with the least probability of error, it was pointed out how desirable it was that they should, whenever possible, be prepared by two independent methods, so selected that there could be no doubt as to the constitution of the resulting product.

If, then, the two preparations of the substance are found to agree substantially in chemical and physical properties, it may be assumed that the values obtained correctly represent the characteristics of that substance. In the communication referred to, the substances studied were  $\Delta^3$ -menthenol(8) and  $\Delta^{3:8(9)}$ -*p*-menthadiene,

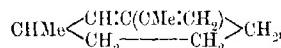
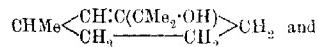


and the influence exerted by the proximity of the double linking to the group  $>\text{CMe}_2 \cdot \text{OH}$  in the menthenol, and especially the high values resulting from the conjugated position of the double linkings in the case of the menthadiene, were discussed in some detail.

Shortly afterwards Luff and Perkin (Trans., 1910, 97, 2147; compare *ibid.*, 1905, 87, 1099) described a method by which  $\Delta^3$ -*m*-menthenol(8) and  $\Delta^{3:8(9)}$ -*m*-menthadiene,



could be obtained in much larger quantity than had previously been possible, and although, so far, only this one method is available for the preparation of these substances, there can be little doubt that they were so pure that the determination of their physical and other properties may be accepted as accurate. The present communication deals with the characteristics of  $\Delta^3$ -*m*-menthenol(8) and  $\Delta^{2:8(9)}$ -*m*-menthadiene,

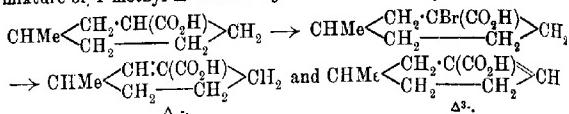


and the results are of special interest in view of the close relationship of these substances with the  $\Delta^3$ -isomerides just mentioned.

$\Delta^2$ -*m*-Menthenol(8) and  $\Delta^{2:8(9)}$ -*m*-menthadiene were first obtained in 1905 by Perkin and Tattersall (Trans., 87, 1101) from 1-methylcyclohexan-3-carboxylic acid (hexahydro-*m*-toluic acid).

This acid was first converted into 3-bromo-1-methylecyclohexan-3-

carboxylic acid, and then, by elimination of hydrogen bromide, into a mixture of 1-methyl- $\Delta^3$ - and  $\Delta^3$ -cyclohexene-3-carboxylic acids,

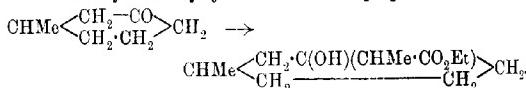


of which the former ( $\Delta^3$ ) is produced in by far the larger proportion. When the ester of 1-methyl- $\Delta^2$ -cyclohexene-3-carboxylic acid was treated with magnesium methyl iodide, it yielded *dl*- $\Delta^2$ -*m*-menthenol(8), which was decomposed by heating with potassium hydrogen sulphate with the formation of *dl*- $\Delta^{2(89)}$ -*m*-menthadiene.

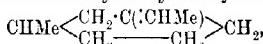
We have now modified the conditions of experiment, and, as the result, have been able to prepare these two *dl*-substances in quantity sufficient to allow of their careful purification and examination, and their physical and chemical properties are summarised in the table given on pp. 122, 123.

A second method, similar in many ways to that employed in the case of the synthesis of  $\Delta^3$ -*p*-menthenol(8) and  $\Delta^{3(89)}$ -*p*-menthadiene from 4-acetyl-1-methyl- $\Delta^3$ -cyclohexene (Perkin and Wallach, Trans., 1910, 97, 1432), has led to the synthesis of the *d*-modifications of  $\Delta^2$ -*m*-menthenol(8) and  $\Delta^{2(89)}$ -*m*-menthadiene.

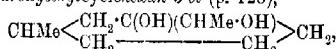
The starting point is *d*-1-methylcyclohexan-3-one, which, as Wallach has shown (Annalen, 1896, 289, 337), is easily obtained in quantity by the hydrolysis of pulegone, and has  $[\alpha]_D + 12.5^\circ$ . Wallach and Evans (Annalen, 1908, 360, 51) had already observed that this ketone reacts with zinc and ethyl  $\alpha$ -bromopropionate with the formation of ethyl 1-methylcyclohexan-3-ol-3- $\alpha$ -propionate,



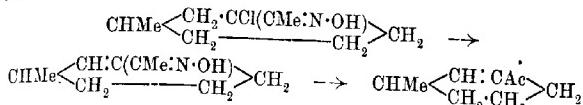
In the present communication it is shown that 1-methylcyclohexan-3-ol-3- $\alpha$ -propionic acid is decomposed on distillation under ordinary pressures and in an atmosphere of hydrogen, with elimination of water and formation of *l*-1-methyl-3-*ethylidenecyclohexane*,



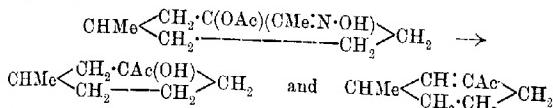
which has  $[\alpha]_D - 50^\circ$ , reversal of rotation having taken place during its formation from *d*-1-methylcyclohexan-3-one. This interesting hydrocarbon yields a *nitroso-chloride* (m. p.  $114^\circ$ ) and a *nitropiperidide* (m. p.  $102^\circ$ ), and, when oxidised by permanganate, it is converted into 1-methyl-3- $\alpha$ -hydroxyethylcyclohexan-3-ol (p. 128),



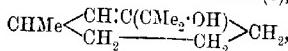
which is crystalline and melts at 68°. The nitroso-chloride of *D*-1-methyl-3-ethylidene-cyclohexane reacts readily when boiled with sodium acetate in acetic acid solution, with elimination of hydrogen chloride and formation of the *oxime* of *d*-3-acetyl-1-methyl- $\Delta^2$ -cyclohexene, which melts at 79° and, when hydrolysed with mineral acids, yields the ketone :



this distils at 212° and has  $[\alpha]_D + 100.4^\circ$ , reversal of rotation having again taken place. The action of sodium acetate and acetic acid on the nitroso-chloride proceeds in another direction at 65° with separation of sodium chloride and formation of the *oxime* of 3-acetoxy-3-acetyl-1-methylcyclohexane, and this, when treated with dilute sulphuric acid, yields a mixture of 3-acetyl-1-methylcyclohexan-3-ol and 3-acetyl-1-methyl- $\Delta^2$ -cyclohexene :

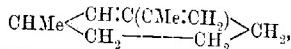


*d*-3-Acetyl-1-methyl- $\Delta^2$ -cyclohexene reacts readily with magnesium methyl iodide, and the resulting *d*- $\Delta^2$ -m-menthenol(8),

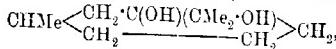


distils at 103–105°/22 mm., has  $[\alpha]_D + 55.6^\circ$ , and yields a phenylurethane, which melts at 124°; its constitution was controlled by oxidation with permanganate, when it was found to yield  $\alpha$ -methyl-adipic acid.

This menthenol is readily decomposed by shaking with dilute sulphuric acid at the ordinary temperature, with loss of water and formation of *d*- $\Delta^2$ -m-mentha-diene,



which distils at 181°/736 mm., and has  $[\alpha]_D + 64.0^\circ$ . The corresponding *terpin* (1-methyl-3- $\alpha$ -hydroxyisopropylcyclohexan-3-ol),



a crystalline substance which melts at 64°, was obtained from *d*-3-acetyl-1-methylcyclohexan-3-ol (p. 132) by treatment with the Grignard reagent.

Although prepared by such widely differing methods, it was interesting to find that the properties of *d*- $\Delta^2$ -m-menthenol(8) and

*d*- $\Delta^{2,5(9)}$ -*m*-menthadiene approximate very closely to, if they do not actually coincide with, those of the corresponding *dl*-isomerides.

The careful consideration of the experimental results described in this communication shows that they confirm and amplify certain deductions as to the general behaviour and properties of menthenols and menthadienes which were discussed in some detail on a previous occasion (Perkin and Wallach, Trans., 1910, 97, 1427). A complete discussion of this interesting subject would take up too much space, but the following points may be briefly emphasised.

$\Delta^2$ - and  $\Delta^2$ -*m*-Menthenol(8) and  $\Delta^3$ -*p*-Menthenol(8) all contain the grouping  $\text{>} \text{C}(\text{CMe}_2)\text{OH}$ , that is to say, they contain an ethenoid linking in direct conjunction with the ' $\text{CMe}_2\text{OH}$ ' group, and the influence of this conjunction may be gathered from the following summary of the more important physical and chemical properties of the (*dl*)-substances:

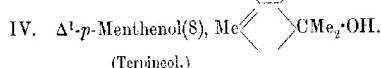
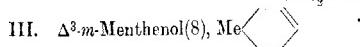
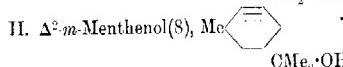
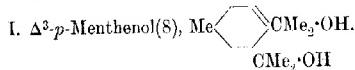


TABLE I.

	I.	II.	III.	IV.
B. p. ....	205°	110°/30 mm.	102°/14 mm.	124°/30 mm.
M. p. ....	39	—	—	35°
<i>d</i> 20/20° ....	0.921	0.9281	0.9288	0.938
<i>n</i> <sub>D</sub> ....	1.4764	1.4772	1.4798	1.4829
M. (calc. 47.16) ....	47.2	16.9	47.10	46.8
M. p. of phenylurethane* ....	128°	127°	130°	113°

\* The phenylurethanes have been added in order to make the table more valuable for purposes of identification.

It is evident from this table that the approach of the ethenoid linking to the ' $\text{CMe}_2\text{OH}$ ' group, whilst it has a tendency to cause a fall in boiling point, density, and refractive index, does not produce any very striking effect on the physical properties of the substance.

When, however, the properties of the corresponding menthadienes are tabulated, it is at once obvious that the effect of the conjugated group  $\text{>} \text{C}(\text{CMe}_2)\text{CH}_2$ , or, in other words, the effect of the approach of the ethenoid linking to the ' $\text{CMe}_2\text{CH}_2$ ' group, is very marked.

The numbers in table II refer to the following substances :

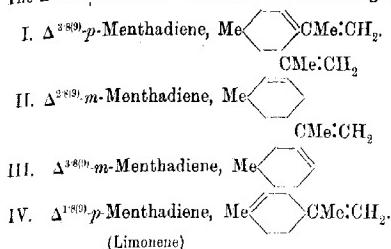
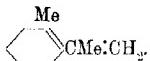


TABLE II.

	I.	II.	III.	IV.
B. p. ....	185°	182°	182°	176°
d 20/20° ....	0.858	0.8624	0.8609	0.846
$n_p$ ....	1.4924	1.5030	1.4975	1.4746
M .....	46.0	46.6	46.3	45.2
(Calc.) $\bar{f}^2 =$	45.24			

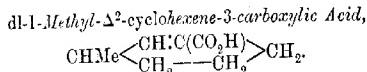
The consideration of these figures brings out very clearly the fact that, in the cases I, II, and III, which are now available for comparison, the effect of conjugation is to raise boiling point, density, and especially refractive index to a remarkable degree above the corresponding values of limonene (IV), but the position of the methyl group in relation to the group  $\text{>} \text{C-CMe:CH}_2$  does not appear to have any distinct effect on these values.

It has been repeatedly pointed out (compare Trans., 1905, 87, 641) that menthadienes containing conjugated ethenoid linkings have also well characterised chemical properties; they are, for example, only capable of combining with two atoms of bromine or one molecule of hydrogen chloride, whereas others, for example, limonene and carvestrene, in which the ethenoid linkings are not conjugated, yield additive compounds with four atoms of bromine and two molecules of hydrogen chloride. The effect of conjugation in the case of an *o*-menthadiene,  $\Delta^{1(8)}\text{-}o$ -menthadiene,



for example, on physical properties has still to be investigated, but, since it has already been observed (Trans., 1905, 87, 1077) that this terpene is only capable of combining with two atoms of bromine, it is highly probable that, in physical properties also, it will exhibit a similar behaviour to that of the conjugated *m*- and *p*-menthadienes (I, II, and III) which have just been discussed.

## EXPERIMENTAL.



The 1-methylecyclohexan-3-carboxylic acid required for these experiments was prepared essentially according to the method already described (Perkin and Tattersall, Trans., 1905, 87, 1091), and then converted into 3-bromo-1-methylecyclohexan-3-carboxylic acid in the following manner. The pure acid (50 grams) was treated with phosphorus pentachloride (76 grams), at first at the ordinary temperature and then on the water-bath, and when conversion into the acid chloride was complete, bromine (60 grams) was added and the whole heated in a reflux apparatus on the water-bath for ten hours.

The product was poured in a thin stream into alcohol (250 c.c.), and, after twenty-four hours, water was added, the bromo-ester extracted with ether, the ethereal solution well washed, very carefully dried, and evaporated.

In order to convert the bromo-ester into the mixed esters of 1-methyl- $\Delta^2$ - and 1-methyl- $\Delta^3$ -cyclohexene-3-carboxylic acids, it was heated, in quantities of 30 grams, with five times its volume of diethylaniline in a reflux apparatus to boiling for five hours.

Sufficient dilute hydrochloric acid was then added to dissolve the diethylaniline, the ester extracted with ether, the ethereal solution washed with sodium carbonate, evaporated, and the residue fractionated, when almost the whole quantity passed over at 145–150°/100 mm.

This was hydrolysed with excess of methyl-alcoholic potassium hydroxide on the water-bath, water was then added, the alcohol removed by evaporation, the acid precipitated by hydrochloric acid, extracted with ether, and distilled in steam. The steam distillate was boiled with excess of freshly precipitated calcium carbonate, filtered, the filtrate evaporated until long hairs began to separate, and then allowed to cool. The characteristic voluminous calcium salt was collected, together with further crops of the same salt obtained by concentrating the mother liquor. It was mentioned in the previous communication (*loc. cit.*, p. 1096) that it is not easy to recrystallise this salt in the usual manner, and to get over this difficulty, the acid was regenerated from the salt by hydrochloric acid, distilled in steam, and again converted into the calcium salt, in order to remove any traces of the  $\Delta^3$ -acid; this treatment was repeated three times. Lastly, the pure salt was decomposed, the acid extracted with ether, and distilled, when it boiled constantly at 150°/11 mm., and when cooled in a freezing mixture showed no signs of crystallising.

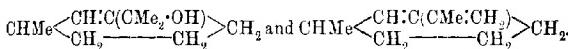
On the first occasion (*loc. cit.*, p. 1096) a small quantity of the pure  $\Delta^2$ -acid was isolated from the mother liquors of the calcium salt of the  $\Delta^2$ -acid, but, under the conditions described above, hardly any of this acid appears to be produced. The separation of the  $\Delta^2$ - and  $\Delta^3$ -isomerides, which seems to be complete, was at first thought to depend on difference in solubility of the calcium salts; that this is not the only reason, and that the separation depends also on the fact that the salt of the  $\Delta^2$ -acid is present in much the larger quantity than that of the  $\Delta^3$ -isomeride, seems to be very probable. In order to test this point, the calcium salt of 1-methyl- $\Delta^3$ -cyclohexene-3-carboxylic acid (m. p. 58–60°; compare Trans., 1910, 97, 2151) was prepared by boiling the acid with water and calcium carbonate. On concentrating the solution, the calcium salt separated in needles and had a somewhat similar appearance to the calcium salt of the  $\Delta^2$ -acid, and there did not appear to be any striking difference in the relative solubilities of the two salts. The calcium salt of the  $\Delta^3$ -acid was collected, washed, and left on porous porcelain exposed to the air for ten days; it then yielded on analysis numbers which agree approximately with those required by the formula  $(C_8H_{11}O_2)_2Ca \cdot 5H_2O$ :

1.0038, dried at 130° until constant, lost 0.2149 and yielded 0.3375

$CaSO_4$ ;  $Ca = 9.8$ ;  $H_2O = 21.4$ .

$(C_8H_{11}O_2)_2Ca \cdot 5H_2O$  requires  $Ca = 9.8$ ;  $H_2O = 22.1$  per cent.

*Dl- $\Delta^2$ -m-Menthanol(8) and Dl- $\Delta^{2,8(9)}$ -m-Menthadiene,*



The following conditions give a more satisfactory yield of  $\Delta^2$ -m-menthenol(8) than those originally employed (Trans., 1905, 87, 1099). Ethyl 1-methyl- $\Delta^2$ -cyclohexene-3-carboxylate (20 grams) is added to an ethereal solution of magnesium methyl iodide (containing 10 grams of magnesium), the solution allowed to remain for two days, then mixed with water, and distilled in steam. The distillate is extracted with ether, the ethereal solution dried over anhydrous sodium sulphate, evaporated, and the residue distilled under diminished pressure:

0.1277 gave 0.3643  $CO_2$  and 0.1349  $H_2O$ .  $C = 77.8$ ;  $H = 11.8$ .

$C_{10}H_{15}O$  requires  $C = 77.9$ ;  $H = 11.7$  per cent.

*Dl- $\Delta^2$ -m-Menthanol(8)* distils at 110°/30 mm., and is a rather viscid, colourless oil, which possesses in a marked degree the pleasant odour of terpineol and menthol characteristic of substances of this class. The determination of its physical properties gave:  $d\ 20/20^\circ = 0.9281$ ,  $n_D = 1.4772$ ,  $M = 46.9$  (calc. 47.16), and it will be observed that

these correspond closely with the values found in the case of *d*- $\Delta^2$ -*m*-menthenol(8) (compare p. 130).

The phenylurethane is readily obtained by mixing the menthenol with the calculated quantity of phenyl carbimide and leaving for several days; the crystalline mass was drained on porous porcelain and crystallised from dilute methyl alcohol:

0·1016 gave 4·7 c.c. N<sub>2</sub> at 18° and 755 mm. N = 5·3.  
 $C_{17}H_{25}O_2N$  requires N = 5·1 per cent.

This phenylurethane separates from methyl alcohol as a felted mass of long needles, and, when quickly heated, melts and decomposes at 127°. That it has the same constitution as the phenylurethane of *d*- $\Delta^2$ -*m*-menthenol(8) is shown by the fact that the mixture of both melts at the same temperature as the constituents.

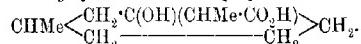
*dl*- $\Delta^{2,5(9)}$ -*m*-Menthadiene.—This terpene is readily obtained by digesting  $\Delta^2$ -*m*-menthenol(8) with 6 per cent. oxalic acid in a reflux apparatus for six hours, and then distilling in steam. The distillate was extracted with ether, the ethereal solution dried, evaporated, and the terpene distilled three times over sodium:

0·1061 gave 0·3425 CO<sub>2</sub> and 0·1140 H<sub>2</sub>O. C = 88·0; H = 11·9.  
 $C_{10}H_{16}$  requires C = 88·2; H = 11·8 per cent.

*dl*- $\Delta^{2,5(9)}$ -*m*-Menthadiene distils at 182—183°/770 mm., and possesses a very pungent odour of lemons, quite distinct, however, from that of limonene; it gives an intense methylene-blue coloration when a drop of sulphuric acid is added to its solution in acetic anhydride.

The determination of the usual physical properties gave: *d* 20/20° = 0·8624, *n*<sub>D</sub> = 1·5030, M = 46·6 (calc. 45·24), and it will be seen that these agree closely with the values observed in the case of *d*- $\Delta^{2,5(9)}$ -*m*-menthadiene (p. 131). It had already been shown (*loc. cit.*, p. 1101) that the *dl*-terpene is only capable of combining with two atoms of bromine, and we have now found that it yields an additive derivative with only 1 molecule of hydrogen chloride.

1-Methylcyclohexan-3-ol-3-*a*-propionic Acid,



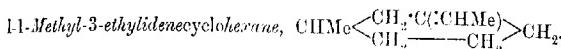
The ester of this acid was first prepared by Wallach and Evans (*Annalen*, 1908, 360, 51) from *d*-1-methylcyclohexan-3-one (from pulegone) by condensation with ethyl bromoacetate and zinc. In order to obtain the ester as pure as possible, the ketone was converted into the semicarbazone and this decomposed by mixing with dilute sulphuric acid and distilling in steam. During the hydrolysis of the ester by methyl-alcoholic potassium hydroxide, some decomposition

with regeneration of a small quantity of the ketone was observed, and this was removed by the addition of water and extraction with ether. The alkaline solution was acidified with dilute sulphuric acid, extracted with ether, the ethereal solution well washed, dried, and evaporated, and the residue left for a fortnight to crystallise. The crystals of 1-methylcyclohexan-3-ol-3-a-propionic acid after draining on porous porcelain, melted not quite sharply at 65°, but, as the acid is very readily soluble in the usual organic solvents and consequently difficult to recrystallise, it was used in this condition in all the subsequent experiments.

The analysis of the silver salt yielded the following result:

0·1905 gave 0·0637 Ag. Ag = 33·4.

$C_{10}H_{17}O_3Ag$  requires Ag = 33·3 per cent.



When 1-methylcyclohexan-3-ol-3-a-propionic acid is heated under the ordinary pressure and in an atmosphere of hydrogen, it is readily decomposed with elimination of water and carbon dioxide, and the above hydrocarbon distils over. The crude product is mixed with a little sodium hydroxide and distilled in steam,\* the distillate is extracted with ether, and the hydrocarbon distilled several times over sodium. 11-Methyl-3-ethylidenecyclohexane has the following physical properties: b. p. 152°, d 19/19° 0·8135,  $n_b$  1·4590, M 41·67 (cale. 41·04),  $[\alpha]_D - 50^\circ$ .

The nitroso-chloride.—This derivative is prepared by mixing the hydrocarbon (10 c.c.) with glacial acetic acid (10 c.c.) and ethyl nitrite (10 c.c.), and adding from a dropping funnel, concentrated hydrochloric acid (5 c.c.) and glacial acetic acid (10 c.c.). After keeping for an hour, the nitroso-chloride is collected, washed with dilute alcohol or ether, left in contact with porous porcelain until dry, and then crystallised from acetone, from which it separates in colourless prisms, melting at 114°:

0·1200 gave 0·0916 AgCl. Cl = 18·9.

$C_9H_{16}ONCl$  requires Cl = 18·7.

The nitropiperidine, prepared from the nitroso-chloride by the action of piperidine, separates from methyl alcohol in colourless needles, and melts at 101—102°:

0·1016 gave 11·0 c.c. N<sub>2</sub> at 21° and 744 mm. N = 12·0.

$C_{14}H_{26}ON_2$  requires N = 11·8 per cent.

\* The alkaline residue, on acidifying and extracting with ether, yields a mixture of unchanged hydroxy-acid and unsaturated acid, which may be employed in a subsequent preparation of the hydrocarbon.

*Oxidation of 1-1-Methyl-3-ethylidenecyclohexane to 1-methyl-3-a-hyd. oxyethylcyclohexan-3-ol.*—In carrying out this oxidation, the pure hydrocarbon (5 grams) was mixed with ice and mechanically shaken with a 1 per cent. solution of permanganate (12·7 grams KMnO<sub>4</sub>). When the product was distilled in steam, a small quantity of unchanged hydrocarbon passed over, but no trace of 1-methylcyclohexan-3-one could be detected, the absence of this ketone being probably due to the fact that it is more readily oxidised than the hydrocarbon. The filtrate and washings of the manganese precipitate were evaporated to a small bulk, extracted with chloroform,\* the chloroform extract dried over potassium carbonate and evaporated, when a syrup remained which soon crystallised. After contact with porous porcelain, the substance was crystallised from water or light petroleum, and thus obtained in colourless, silky needles, melting at 68°:

0·0918 gave 0·2288 CO<sub>2</sub> and 0·0928 H<sub>2</sub>O. C = 68·0; H = 11·2.  
C<sub>9</sub>H<sub>18</sub>O<sub>2</sub> requires C = 68·3; H = 11·3 per cent.

When this glycol is digested with dilute sulphuric acid, it yields a ketone which appears to be 3-acetyl-1-methyl-Δ<sup>2</sup>-cyclohexene.



The oxime of this ketone is produced when the nitroso-chloride of l-1-methyl-3-ethylidenecyclohexane (10 grams) is mixed with anhydrous sodium acetate (10 grams) and glacial acetic acid (40 c.c.) and gently warmed with a small flame, and afterwards boiled for about ten minutes, during which, sodium chloride separates. The product is cooled, diluted with water, made alkaline with ammonia, and the crude oxime, which separates as a brown oil, extracted with ether. The ethereal solution is dried, evaporated, and the residue distilled under diminished pressure, when a colourless oil passes over at 140—150°/20 mm., which crystallises. After draining on porous porcelain, the oxime separated from ether or methyl alcohol in prisms melting at 79°:

0·0672 gave 5·7 c.c. N<sub>2</sub> at 22° and 741 mm. N = 9·3.  
C<sub>9</sub>H<sub>15</sub>ON requires N = 9·2 per cent.

The benzoyl derivative was obtained by adding benzoyl chloride to the solution of the oxime in dilute sodium hydroxide, and crystallises from methyl alcohol in long needles melting at 85—86°:

0·1095 gave 5·7 c.c. N<sub>2</sub> at 21° and 751 mm. N = 5·6.  
C<sub>16</sub>H<sub>18</sub>O<sub>2</sub>N requires N = 5·4 per cent.

\* The aqueous solution yields, on acidifying and extracting with ether, a mixture of methyl adipic acids.

d-3-Acetyl-1-methyl- $\Delta^2$ -cyclohexene is obtained from the crude oxime, by mixing with dilute sulphuric acid and distilling in steam.

The distillate is extracted with ether, the ethereal solution evaporated, and the crude ketone purified by conversion into the semicarbazone by means of semicarbazide hydrochloride and sodium acetate in the usual way. The crystalline mass thus obtained is a mixture of two semicarbazones, and is separated into its constituents by fractional crystallisation from alcohol. The less soluble constituent is the semicarbazone of d-3-acetyl-1-methyl- $\Delta^2$ -cyclohexene and melts at 219°:

0.1046 gave 0.2365 CO<sub>2</sub> and 0.0822 H<sub>2</sub>O. C = 61.6; H = 8.7.

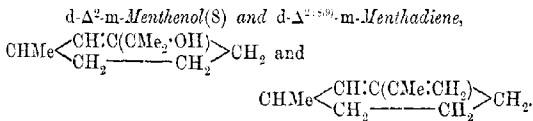
C<sub>10</sub>H<sub>17</sub>ON<sub>2</sub> requires C = 61.5; H = 8.7 per cent.

The more readily soluble constituent is the semicarbazone of 3-acetyl-1-methylcyclohexan-3-ol (m. p. 119°, p. 131). The semicarbazone of melting point 219° is decomposed with dilute sulphuric acid, and the ketone distilled in steam, extracted with ether, and fractionated under the ordinary pressure, when it boils constantly at 210—212°, and has an odour resembling that of menthone and cyclohexanone:

0.1334 gave 0.3821 CO<sub>2</sub> and 0.1252 H<sub>2</sub>O. C = 78.1; H = 10.4.

C<sub>9</sub>H<sub>14</sub>O requires C = 78.2; H = 10.1 per cent.

The physical properties of this ketone are as follows: b. p. 210—212°, d 22/22° 0.9413, n<sub>D</sub> 1.4817, M 41.77, [α]<sub>D</sub> +100.4°, and it is interesting to compare these values with the corresponding properties of 4-acetyl-1-methyl- $\Delta^1$ -cyclohexene and 4-acetyl-1-methyl- $\Delta^2$ -cyclohexene, the properties of which have been tabulated in a previous paper (Trans., 1910, 97, 1432). It will also be observed that the rotation (-50°) of l-1-methyl-3-ethylidene-cyclohexane has become dextro (+100.4°) during the conversion into the ketone,



In order to prepare the former of these substances, pure 3-acetyl-1-methylcyclohexene was added to an excess of an ethereal solution of magnesium methyl iodide, and, after keeping for one hour and heating on the water-bath for one hour, the product was decomposed by water and distilled in steam. The distillate was extracted with ether, the ethereal solution dried over potassium carbonate, evaporated, and the colourless residue distilled under diminished pressure:

0.0956 gave 0.2730 CO<sub>2</sub> and 0.1017 H<sub>2</sub>O. C = 77.9; H = 11.8.

C<sub>10</sub>H<sub>15</sub>O requires C = 77.9; H = 11.7 per cent.

The physical properties of *d*- $\Delta^2$ -*m*-menthenol(8) are the following: b.p. 206–208°/760 mm. or 103–105°/22 mm., *d* 22/22° 0.923, *n*<sub>D</sub> 1.4738, M 47.21 (calc. 47.16), [α]<sub>D</sub> +55.56°. The *phenylurethane*, prepared in the usual manner, separated from methyl alcohol in long, colourless needles, and melted at 124°. A comparison of these properties with those of *dl*- $\Delta^2$ -*m*-menthenol(8) (p. 125) shows that, although the values are not identical, they correspond very closely.

*Oxidation of d*- $\Delta^2$ -*m*-Mentheneol(8) to  $\alpha$ -Methyladipic Acid.

In investigating this degradation, the menthenol (1.5 grams) was oxidised with a 2 per cent. solution of permanganate (4.2 grams) at 0°, and then any unchanged menthenol removed by distillation in steam. The filtrate and washings of the manganese precipitate were concentrated and extracted with ethyl acetate, but only traces of a neutral substance (glycol) were left on evaporation. The alkaline solution was acidified, several times extracted with ether, the ethereal solution dried and evaporated, when a solid acid remained, which proved to be very difficult to crystallise. It was dissolved in dry ether and saturated with ammonia, when a crystalline salt separated, and by the addition of copper sulphate, this was converted into the blue copper salt, which was collected, washed, and dissolved in dilute hydrochloric acid. After removing the copper by hydrogen sulphide, the filtrate was evaporated, and the concentrated solution kept over solid potassium hydroxide in a vacuum desiccator, when a solid acid remained, which separated from a mixture of benzene and light petroleum as a crystalline powder, melting at 65–66°. The silver salt was analysed:

0.0370 gave 0.0212 Ag. Ag = 57.3.

$C_7H_{10}O_4Ag_2$  requires Ag = 57.7 per cent.

There can be no doubt that this acid is  $\alpha$ -methyladipic acid, which Bone and Perkin (Trans., 1895, 67, 115) found to melt at 64°.

*d*- $\Delta^{2(4)}$ -*m*-Menthadiene.—This terpene is readily obtained when *d*- $\Delta^2$ -*m*-menthenol(8), in quantities of 5 grams, is shaken mechanically with 500 c.c. of 1.5 per cent. sulphuric acid for a week, and the product neutralised with sodium carbonate and distilled in steam.\*

The distillate is extracted with ether, the ethereal solution carefully dried, evaporated, and the hydrocarbon distilled several times over sodium, when it boiled constantly at 181°/736 mm., and had an odour different from that of limonene, but somewhat resembling that of sylvestrene. The analysis and determination of the usual physical

\* The residue in the steam distillation flask was concentrated and several times extracted with ethyl acetate without, however, yielding a trace of the terpin.

constants gave the following results (compare the corresponding values of *d*- $\Delta^{2:8(9)}$ -*m*-menthadiene, p. 126) :

0·0953 gave 0·3084 CO<sub>2</sub> and 0·1028 H<sub>2</sub>O. C = 88·2; H = 12·0.

C<sub>10</sub>H<sub>16</sub> requires C = 88·2; H = 11·8 per cent.

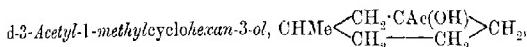
*d* 17/17° 0·864, *n*<sub>D</sub> 1·4946, M 45·87 (calc. 45·24), [α]<sub>D</sub> + 64·0°.

The solution of the terpene in acetic anhydride gives, on the addition of sulphuric acid, an intense blue-violet coloration, which gradually changes to red.

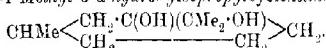
The dihydrochloride of *d*- $\Delta^{2:8(9)}$ -*m*-menthadiene is obtained when *d*- $\Delta^2$ -*m*-menthenol(8), dissolved in three times its volume of glacial acetic acid, is cooled in a freezing mixture and saturated with hydrogen chloride. On keeping, an oil separates at the surface, and, after adding ice, the heavy oil is extracted with ether, the ethereal solution washed with sodium carbonate, dried, evaporated, and the residue distilled under diminished pressure, when it passes over at 110—115°/12 mm., slight loss of hydrogen chloride taking place during the distillation :

0·1582 gave 0·1930 AgCl. Cl = 30·2.

C<sub>10</sub>H<sub>18</sub>Cl<sub>2</sub> requires Cl = 34·0 per cent.



and *d*-1-Methyl-3-*a*-hydroxyisopropylcyclohexan-3-ol,



It has already been stated (p. 128) that the nitroso-chloride of *l*-1-methyl-3-ethylidene cyclohexene is decomposed by boiling with sodium acetate and acetic acid for a few minutes with formation of the oxime of 3-acetyl-1-methyl- $\Delta^2$ -cyclohexene. If, instead of boiling, the mixture is kept at 65° for fifteen minutes, the reaction proceeds somewhat differently, and, beside the above oxime, there is formed as the principal product the acetyl derivative of the oxime of 3-acetyl-1-methylcyclohexene-3-ol, which is a viscid gum. This was hydrolysed by treatment with dilute sulphuric acid (2 per cent.) and distillation in steam, and the distillate yielded, on extraction with ether, an oil which was converted into the mixed semicarbazones of melting points 199° and 219° by treatment with sodium acetate and semicarbazide hydrochloride (p. 129). These were separated by fractional crystallisation from alcohol, and the semicarbazone of *d*-3-acetyl-1-methylcyclohexan-3-ol (m. p. 199°) was analysed :

0·0938 gave 0·1946 CO<sub>2</sub> and 0·0768 H<sub>2</sub>O. C = 56·5; H = 9·0.

C<sub>10</sub>H<sub>15</sub>O<sub>2</sub>N<sub>3</sub> requires C = 56·3; H = 8·9 per cent.

The hydroxy-ketone is obtained from this semicarbazone by treat-

ment with dilute sulphuric acid, and is readily decomposed by boiling with dilute acids with elimination of water and formation of 3-acetyl-1-methyl- $\Delta^2$ -cyclohexene (p. 128).

*d*-1-Methyl-3-*a*-hydroxyisopropylcyclohexan-3-ol is obtained when 3-acetyl-1-methylcyclohexan-3-ol is treated with magnesium methyl iodide, but it is most conveniently prepared by treating the mixture of ketones, obtained as explained on p. 129, with this reagent.

When the product is fractionated under diminished pressure, *d*. $\Delta^2$ -*m*-menthol(8) passes over first, and then a considerable quantity of a syrup distils at about 140°/23 mm., and, on cooling, solidifies.

This substance was left in contact with porous porcelain until quite free from oil, and then crystallised from light petroleum:

0·1063 gave 0·2721 CO<sub>2</sub> and 0·1130 H<sub>2</sub>O. C = 69·8; H = 11·8.

C<sub>10</sub>H<sub>20</sub>O<sub>2</sub> requires C = 69·8; H = 11·6 per cent.

*d*-1-Methyl-3-*a*-hydroxyisopropylcyclohexan-3-ol melts at 64°, is readily soluble in water, and is an interesting substance, because it is the terpin corresponding with *d*. $\Delta^{2\text{,80}}$ -*m*-menthadiene.

THE UNIVERSITIES OF GÖTTINGEN AND MANCHESTER.

## XVI.—*The Direct Action of Radium on Ammonia.*

By EDGAR PHILIP PERMAN.

EXPERIMENTS have been made by Ramsay (*Trans.*, 1908, **93**, 96), and more recently by Usher (*Trans.*, 1910, **97**, 389), on the decomposition of ammonia by radium emanation. I have now tried the effect of the direct action of radium bromide, as it seemed possible that such experiments might facilitate the interpretation of the results obtained with the emanation. The apparatus employed consisted of two cylindrical bulbs, *A*, *B*, each of about 50 c.c. capacity, connected by capillary tubing, and a gauge tube, *C*, of 5 mm. diameter. Five milligrams of pure radium bromide were placed in a glass capsule at the lower end of *A*. The whole apparatus was then filled with ammonia through one of the side tubes, *D*, *E*, by repeated exhaustion and admission of ammonia. Mercury was introduced into the gauge, and the side tube sealed off, leaving the gas in each bulb under the atmospheric pressure. The bulbs were maintained at the same temperature by placing them in a dish of water, the gauge alone projecting. A mirror scale was fixed behind the gauge, and readings were taken every few days. At first the pressure in *A* decreased, as found by Ramsay with the emanation;

FIG. 1.

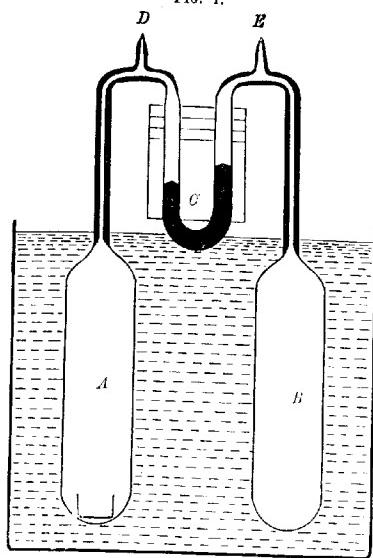
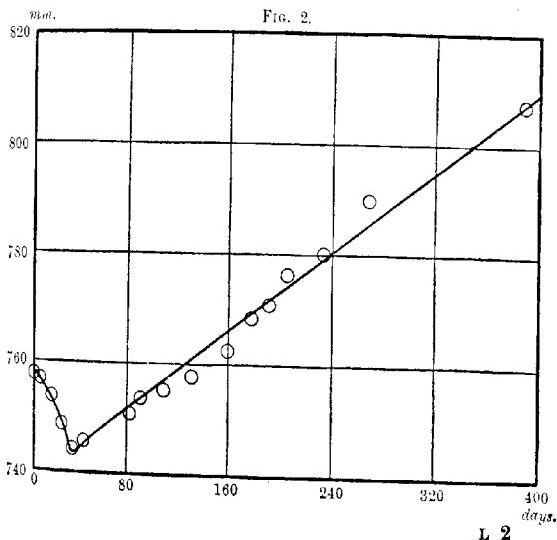


FIG. 2.



L 2

this continued for about five weeks, when a steady increase began. The pressures are given in the following table; they are calculated from the readings of the gauge, and the volumes of the bulbs *A*, *B*, corrections being made for the volumes of the connecting tubes:

Time.	$\Delta p$ .	Pressure in bulb containing radium.
0 days	0·0 mm.	757·7 mm.
6 "	-0·5 "	756·9 "
16 "	-2·5 "	753·7 "
25 "	-5·6 "	748·5 "
35 "	-8·7 "	743·9 "
44 "	-7·6 "	745·4 "
82 "	-4·3 "	750·7 "
91 "	-2·5 "	753·7 "
109 "	-1·6 "	755·2 "
131 "	0·0 "	757·7 "
145 "	+1·5 "	760·1 "
159 "	-2·9 "	762·4 "
177 "	-6·7 "	768·3 "
191 "	-8·3 "	770·8 "
205 "	-11·7 "	776·3 "
233 "	-14·2 "	789·3 "
268 "	-20·2 "	789·9 "
389 "	-30·9 "	807·2 "

The first fall of pressure is probably due to the presence of a small quantity of air. Supposing this to be present, the radiations from the radium would decompose some of the ammonia, and the hydrogen would form water with the oxygen of the air. When once the pressure has begun to increase, it increases fairly regularly. This is shown by the curve, which is nearly straight after the increase has begun. It is constructed from the numbers already given.

Before attempting to interpret these results, it was thought advisable to measure, if possible, whether there was any diminution of pressure caused by the gases being driven into the glass by the radiations. An experiment was therefore made with the apparatus as before, but filled with undried air. The following numbers were obtained:

Time.	Fall of pressure in bulb containing radium.	$\Delta p$ .	$\Delta p'$
0 days.	0·0 mm.	—	—
29 "	2·0 "	2 mm.	0·10
31 "	3·9 "	1·9 "	0·17
49 "	6·5 "	2·6 "	0·14
92 "	13·2 "	6·7 "	0·16
116 "	16·7 "	3·5 "	0·15

After the first few days a regular contraction took place, and this showed no sign of falling off even in the course of four months. On opening the tube, it was found that a small globule of mercury had fallen into the capsule containing the radium, and on the sides of the capsule there was a small deposit of mercuric oxide. The

radiations thus caused the oxidation of mercury in the presence of moist air. As it was uncertain what part of the fall of pressure might have been due to absorption of oxygen by the mercury, another experiment was made in a similar way, but filling the bulb with dry nitrogen. The pressure fell as before and at about the same rate:

Time.	Fall of pressure in bulb containing radium.	$\Delta p.$	$\frac{\Delta p}{\Delta t'}$ .
0 days	0.0 mm.	—	—
22 "	2.3 "	2.3 mm.	0.10
35 "	3.9 "	1.6 "	0.12

Thus very little of the effect could have been due to absorption of oxygen, and the increase in pressure obtained in the decomposition of ammonia does not represent the total decomposition. The preliminary fall of pressure in the ammonia experiment is thus partly accounted for, apart from the presence of air. The actual rate of decrease at the beginning of the ammonia experiment was about double that in the nitrogen experiment. As the fall of pressure due to this cause is so large, and, moreover, probably differs for different gases, it is impossible at present to calculate with any exactness the rate of decomposition of ammonia. It would appear, however, to be a reaction of the first order. As a rough approximation, the 5 milligrams of radium bromide decomposed 0.01 milligram of ammonia per day.

UNIVERSITY COLLEGE,  
CARDIFF.

## XVII.- *The Identity of Xanthaline and Papaveraldine.*

By BESSIE DORSON and WILLIAM HENRY PERKIN, jun.

DURING the course of their valuable investigations on the constituents of opium, Messrs. T. and H. Smith (*Pharm. J.*, 1893, p. 793) described the isolation of a colourless alkaloid melting at 206°, which exhibited the characteristic property of forming yellow salts, and was therefore named xanthaline. This substance, which occurs in opium only in minute quantities, was isolated in a pure condition, and analyses of the alkaloid itself, as well as of its hydrochloride and reduction product (hydroxanthaline), seemed to indicate that its formula was  $C_{27}H_{36}O_9N_2$ . With a view to determine its nature, Messrs. T. and H. Smith sent the authors a quantity of this alkaloid, and a portion of it was recrystallised

from methyl ethyl ketone, in which it dissolved very sparingly in the cold, but much more readily on boiling. The hot solution, when allowed to cool slowly, deposits the alkaloid in colourless scales, which melt sharply at 207° or 210° (corr.):

0·1382 gave 0·3444 CO<sub>2</sub> and 0·0686 H<sub>2</sub>O. C=68·0; H=5·5.

0·2398 " 8·3 c.c. N<sub>2</sub> at 16° and 761 mm. N=4·0.

0·3443, heated with hydriodic acid by Perkin's modification of Zeisel's method, yielded 0·8884 AgI. MeO=34·1.

C<sub>20</sub>H<sub>19</sub>O<sub>5</sub>N, containing 4MeO, requires MeO=35·1 per cent.

These numbers agree closely with those obtained by Messrs. T. and H. Smith, who give four analyses of the alkaloid, the mean of which is C=67·8; H=5·6; N=4·3, and it will be seen that these percentages correspond with the formula C<sub>20</sub>H<sub>19</sub>O<sub>5</sub>N, which requires C=68·0; H=5·4; N=3·9 per cent. In order to test the validity of this formula, the authors prepared the *platinichloride* of the alkaloid, which crystallised from dilute hydrochloric acid in orange-red prisms, and yielded, on analysis, the following result:

0·3500 gave 0·0611 Pt. Pt=17·4.

(C<sub>20</sub>H<sub>19</sub>O<sub>5</sub>N)<sub>2</sub>.H<sub>2</sub>PtCl<sub>6</sub> requires Pt=17·4 per cent.

The *methiodide* was next prepared by heating the alkaloid (10 grams) with methyl iodide (10 c.c.) and methyl alcohol (40 c.c.) in a sealed tube in the steam-bath, when the substance, which at first is sparingly soluble, passed completely into solution, and, on cooling, characteristic orange stars separated in quantity on the sides of the tube. The crystals were collected and left exposed to the air for several days, the substance then melted at 132°, and yielded, on analysis, numbers agreeing with the formula C<sub>20</sub>H<sub>19</sub>O<sub>5</sub>N.MeI,3H<sub>2</sub>O:

0·3578, dried at 100°, lost 0·0334 H<sub>2</sub>O=9·3.

0·7204 " 105° " 0·0756 H<sub>2</sub>O=10·5.

0·1570 gave 0·0650 AgI. I=22·4.

C<sub>20</sub>H<sub>19</sub>O<sub>5</sub>N.MeI,3H<sub>2</sub>O requires H<sub>2</sub>O=9·8; I=23·1 per cent.

This methiodide was then recrystallised several times from methyl alcohol, from which it separated in brilliant yellow prisms, which melted at 194°, and had the composition C<sub>20</sub>H<sub>19</sub>O<sub>5</sub>N.MeI,3H<sub>2</sub>O:

0·1089 gave 0·1982 CO<sub>2</sub> and 0·0469 H<sub>2</sub>O. C=49·6; H=4·8.

0·1565 " 0·0710 AgI. I=24·5.

C<sub>20</sub>H<sub>19</sub>O<sub>5</sub>N.MeI,3H<sub>2</sub>O requires C=49·1; H=4·7; I=24·7 per cent.

*Fusion with Potassium Hydroxide.*—In this experiment potassium hydroxide (30 grams) was mixed with water (5 c.c.), just fused in a nickel crucible, and then xanthaline (10 grams) added; the flame was at once removed, and the fusion stirred for two or three minutes, and until the alkaloid was completely decomposed. The crucible was then plunged into hot water, the oil which

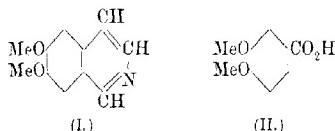
separated extracted with ether, the ethereal solution dried over solid potassium hydroxide and evaporated, when an oil remained which, on exposure to the air, soon solidified. After contact with porous porcelain, the substance was crystallised from ether or light petroleum, from both of which solvents it separated as a colourless, crystalline powder:

0·1112 gave 0·2846 CO<sub>2</sub> and 0·0579 H<sub>2</sub>O. C=69·7; H=5·8.

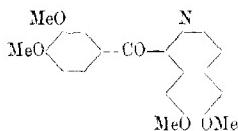
0·1860, " 11·2 c.c. N<sub>2</sub> at 15° and 758 mm. N=7·0. "

C<sub>11</sub>H<sub>11</sub>O<sub>2</sub>N requires C=69·8; H=5·8; N=7·4 per cent.

This substance, which melts at 94·5° and is obtained in a yield of at least 35 per cent., is dimethoxyisoquinoline (I). The alkaline solution, from which this substance had been extracted, yielded, on acidifying, a solid acid, which, after crystallisation from water, melted at 179·5, and was easily recognised as veratric acid (II):



The consideration of all these facts seemed to show that the alkaloid xanthaline most probably has the constitution:



that is to say, that it was identical with papaveraldine, the substance which Goldschmidt (*Monatsh.*, 1885, 6, 956) first obtained by the oxidation of papaverine with permanganate. In order to test this supposition, a quantity of papaveraldine was prepared from papaverine, and the direct comparison proved conclusively that it was identical with xanthaline. Both melted at 208°, and, when intimately mixed, there was no alteration in the melting point. In describing the fusion of papaveraldine with potassium hydroxide, Goldschmidt (*loc. cit.*) does not appear to have observed that dimethoxyisoquinoline is a crystalline substance, but we satisfied ourselves that, when papaveraldine from papaverine is fused with potassium hydroxide under the conditions described above, the dimethoxyisoquinoline obtained crystallises and melts at 94·5°.

It is, of course, impossible to say whether papaveraldine is

actually present in opium, or whether it is formed from papaverine during the complicated treatment which is necessary before it can be separated from the other constituents of opium.

THE UNIVERSITY,  
MANCHESTER.

XVIII.—*Organic Derivatives of Silicon. Part XIV.  
The Preparation of Tertiary Silicols.*

By FREDERIC STANLEY KIPPING and JOHN EDWARD HACKFORD,  
A.I.C., B.Sc.

VARIOUS tertiary silicols,  $R_3Si\cdot OH$ , have been obtained incidentally in the course of these investigations, and have been very briefly described in previous papers. In these cases the compounds were prepared by the hydrolysis of the tertiary chlorides,  $R_3SiCl$ , a method which suffers from the serious disadvantage that the tertiary chlorides are themselves obtained only with considerable difficulty, and, generally speaking, are not easily separated from accompanying by-products.

A procedure promising more satisfactory results was not far to seek. On the presumption that the behaviour of the silicones,  $R_2SiO$ , would be analogous to that of the ketones, it was only necessary to prepare the silicones by the hydrolysis of the dichlorides,  $R_2SiCl_2$  (which are usually obtained much more easily than the trichlorides), and to treat these silicones with a Grignard reagent.

That a silicone would react with a magnesium alkyl or aryl halogen compound giving ultimately a tertiary silicol was, of course, a natural deduction to base on the known relationship of silicon to carbon. On the other hand, the very great dissimilarity between the silicones and the ketones in their general chemical behaviour, which was brought out by a study of benzylethylsilicone (Robison and Kipping, Trans., 1908, 93, 439), pointed to the possibility that this anticipation might not be realised.

As a matter of fact, the silicones were found to react with the Grignard reagents in a normal manner, and it is perhaps hardly too much to say that this is the first instance in which the silicones have been proved to show any analogy to the ketones in chemical behaviour.

Several tertiary silicols were prepared by the method here indicated; the yields were generally satisfactory, and the products, as a rule, did not contain any considerable proportion of the corre-

sponding oxides,  $R_3Si \cdot O \cdot SiR_3$ , into which the silicols are so prone to pass.

The silicones which were used in the earlier experiments were the crude liquid substances which were obtained by the decomposition of the purified dichlorides with water; these silicones, therefore, probably consisted to a considerable extent of the termolecular polymerides,  $(R_2SiO)_3$ . As these preparations gave, nevertheless, good yields of the desired products, it seemed to follow that the termolecular silicones were resolved into the unimolecular compounds by the action of the Grignard reagents. This conclusion was borne out by the results of experiments with the pure termolecular form of dibenzylsilicone, which was found to yield the tertiary silicol,  $SiMe(CH_2C_6H_5)_2 \cdot OH$ , after treatment with magnesium methyl iodide.

It was also found, as was of course to be expected in view of the results just mentioned, that a dihydric silicol, such as dibenzylsilicol,  $Si(CH_2C_6H_5)_2(OH)_2$ , could be converted into a tertiary silicol by the method in question.

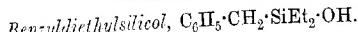
As the relatively very stable termolecular silicones are attacked by the Grignard reagents, and as these polymerides probably contain the grouping  $R_2Si \cdot O \cdot SiR_2$ , it seemed possible that the oxides  $R_3Si \cdot O \cdot SiR_3$  might likewise react with the magnesium compounds, and yield, ultimately, a tertiary silicol and a silicane. Experiments, however, showed that the oxides remained unchanged even after they had been heated strongly with magnesium alkyl bromides.

The above method for the preparation of silicols is applicable, of course, in the case of asymmetric compounds,  $R^1R^2R^3Si \cdot OH$ , as well as in that of symmetrical silicols,  $R^1R^2Si \cdot OH$  and  $R_3Si \cdot OH$ ; the latter, however, it was found, may also be obtained, and perhaps more conveniently, by the interaction of an aryl (or alkyl) derivative of metasilicic acid and a Grignard reagent. Triphenylsilicol, for example, may be prepared by treating phenylmetasilicic acid,  $C_6H_5SiO \cdot OH$ , with magnesium phenyl bromide, and tribenzylsilicol may be obtained from benzylmetasilicic acid in a corresponding manner. As is well known, in preparing tertiary alcohols from carboxylic acids, it is customary to employ the acids in the form of their esters; whether this is necessary or not in the case of the carboxylic acids, it is certainly not so as regards the silicic acids; the latter may be directly treated with the Grignard reagents.

In preparing phenylmetasilicic acid from the trichloride  $SiPhCl_3$ , it was found that hydrolysis with cold or even with hot water gave the acid as a viscous compound which was readily soluble in many organic solvents; hydrolysis with steam, on the other hand, resulted

in the formation of a vitreous solid, which was insoluble in all the common organic solvents and appeared to be the (polymerised) anhydride of the acid.

#### EXPERIMENTAL.



Benzylethylsilicone, obtained by the decomposition of benzylethylsilicon dichloride with water (Trans., 1907, **91**, 720), was carefully dried at  $100^\circ$ , and the oil, which probably consisted partly of the termolecular compound (Robison and Kipping, *loc. cit.*), was then gradually added to an ethereal solution of magnesium ethyl bromide ( $\frac{1}{2}$  mols.). After the ether had been distilled off, the residue was heated at about  $190^\circ$  during one hour. When cold, the product was treated with water, and the oil which separated was extracted with ether and distilled under a pressure of 40 mm. The thermometer rose rapidly to  $165^\circ$ , at which temperature about 60 per cent. of the liquid passed over, and only a small quantity of a residue of high boiling point was obtained. Immediately after redistillation a sample of the liquid, boiling at  $165^\circ/40$  mm., was analysed:

0.5572 gave 0.1698  $SiO_2$ .  $Si=14.3$ .

$C_{11}H_{18}OSi$  requires  $Si=14.6$  per cent.

*Benzylidethylsilicole* is a colourless, mobile liquid, and is miscible with most of the common solvents. In the course of a day the clear, bright silicole became cloudy and deposited globules of water, an indication that it was undergoing a spontaneous transformation into the oxide. This change, however, occurred very slowly, and when redistilled the next day most of the liquid passed over below  $167^\circ/40$  mm.

It was found by Martin and Kipping (Trans., 1909, **95**, 303) that tribenzylsilicole could be converted into tribenzylsilicoyl chloride with the aid of acetyl chloride. If therefore other silicols could be transformed into the corresponding chlorides in a similar manner, these chlorides might then be employed for the preparation of various silicanes by the method previously used for this purpose. In order to test this possibility, benzylidethylsilicole was heated with a large excess of acetyl chloride during three hours, and the product was then distilled. Most of the liquid, excluding the acetyl chloride, passed over from  $155^\circ$  to  $165^\circ/15$  mm., and a small proportion, consisting probably of the oxide, from  $200^\circ$  to  $250^\circ$ .

The fraction of lower boiling point contained only 5 per cent. of combined chlorine ( $C_{11}H_{17}Cl$  contains 16.5 per cent. of chlorine), and was again heated with a large excess of acetyl chloride, but the product did not afford the desired chloride in anything approaching a condition of purity.

*Benzylethylpropylsilicol*,  $C_6H_5\cdot CH_2\cdot SiEtPr\cdot OH$ .

Benzylethylsilicone, prepared in the same way as the sample used in the preceding experiment, was added to an ethereal solution of magnesium propyl bromide ( $1\frac{1}{2}$  mols.). The ether was distilled, and the residue heated at about  $190^\circ$  during one hour. The oily product which separated on the addition of water was extracted with ether and distilled under diminished pressure. Almost the whole of the liquid passed over between  $169^\circ$  and  $174^\circ/40$  mm., and there was very little residue.

The freshly prepared silicol was analysed:

0·3264 gave 0·0964  $SiO_2$ .  $Si = 13\cdot 9$ .

$C_{12}H_{20}OSi$  requires  $Si = 13\cdot 6$  per cent.

This compound has already been described (Kipping, Trans., 1907, **91**, 223), and the observation that the distilled product becomes turbid when kept at the ordinary temperature, with formation of benzylcethylpropylsilicil oxide and water, was confirmed.

*Phenylmethylethylylsilicol*,  $SiMeEtPh\cdot OH$ .

The phenylethylsilicone used in this and the following experiment was prepared by the hydrolysis of phenylethylsilicon dichloride (Marsden and Kipping, Trans., 1908, **93**, 208), and was treated with magnesium methyl iodide in the manner described in previous cases. When the product was distilled under diminished pressure, it yielded a large fraction, boiling constantly at  $115^\circ/17$  mm.

This preparation was immediately analysed:

0·3780 gave 0·1406  $SiO_2$ .  $Si = 17\cdot 5$ .

$C_9H_{14}OSi$  requires  $Si = 17\cdot 0$  per cent.

*Phenylmethylethylylsilicol* is a colourless, mobile liquid, practically insoluble in water. In the course of half an hour, the clear, bright product became distinctly turbid, and drops of water gradually separated, but the transformation into the oxide seemed to be only very partial.

*Phenyldiethylylsilicol*,  $SiEt_2Ph\cdot OH$ .

Phenylethylsilicone was treated with magnesium ethyl bromide under the conditions previously described in other cases, and the product was separated in the usual manner. When distilled under diminished pressure, most of the liquid passed over between  $160^\circ$  and  $170^\circ/60$  mm., and from this fraction the pure silicol was isolated as a colourless, mobile liquid, boiling at  $165^\circ/60$  mm.

An analysis of the freshly prepared substance was made:

0·3438 gave 0·1172 SiO<sub>2</sub>. Si=16·0.

C<sub>10</sub>H<sub>16</sub>OSi requires Si=15·7 per cent.

Like most of the other silcols, this compound became turbid in the course of some hours, and changed spontaneously into the corresponding oxide and water. The product was redistilled after it had been kept for some time, and a fraction boiling at 208–210°/40 mm. was collected; this substance probably consisted of phenyl-diethyldisiloxane, but silicon estimations gave unsatisfactory results, owing to the impossibility of burning away the whole of the carbon.

*Dibenzylmethylsilanol*, SiMe(CH<sub>2</sub>·C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>·OH.

Ternolecular dibenzylsilicono (m. p. 98°), obtained from dibenzylsilicon dichloride by the method already described (Robison and Kipping, Trans., 1908, **93**, 440), was treated with an ethereal solution of magnesium methyl iodide. The ether was distilled, and the residue was heated at about 200° during an hour. The oily product, isolated in the usual manner, when distilled under diminished pressure boiled very constantly at 240–242°/60 mm., and only a small proportion passed over outside these limits. The freshly prepared liquid was analysed:

0·4470 gave 0·1130 SiO<sub>2</sub>. Si=11·9.

C<sub>15</sub>H<sub>18</sub>OSi requires Si=11·7 per cent.

*Dibenzylmethylsilicole* is a colourless, mobile liquid, practically insoluble in water, but miscible with organic solvents.

*Dibenzylmethylsilicyle Oxide*, [SiMe(CH<sub>2</sub>·C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>]<sub>2</sub>O.

The pure silicol just described gradually changed when it was left at the ordinary temperature, and after about a fortnight's time it yielded colourless crystals, which were separated and recrystallised from ether:

0·3414 gave 0·0912 SiO<sub>2</sub>. Si=12·5.

0·3496 „ „ 0·9842 CO<sub>2</sub> and 0·2372 H<sub>2</sub>O. C=76·6; H=7·5.

C<sub>30</sub>H<sub>34</sub>OSi<sub>2</sub> requires Si=12·2; C=77·1; H=7·3 per cent.

These analyses and the manner of formation of this crystalline product show that it is *dibenzylmethylsilicyle oxide*, produced by the spontaneous decomposition of the silicol. It melts at 56°, and is readily soluble in ether, chloroform, or benzene, and moderately easily so in alcohol.

#### *Conversion of Dibenzylsilicol into a Tertiary Silicol.*

The action of magnesium methyl iodide on the β-form of dibenzylsilicol, Si(CH<sub>2</sub>·C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>(OH)<sub>2</sub>, described by Robison and Kipping

(Trans., 1908, **93**, 453), was also investigated. As the first result would probably be the conversion of the dihydric silicol into the silicone and water, a large excess of the Grignard reagent was used. A vigorous reaction occurred at first, and after a procedure described in previous cases a colourless oil was obtained. This product, like that obtained from dibenzylsilicone, boiled very constantly at 240—242°/60 mm., from which fact it was concluded that the oil consisted of dibenzylmethylsilicol. In order to hasten the change into the oxide, the sample was heated at its boiling point under atmospheric pressure during about an hour, and was then allowed to cool. The next morning the sample was a pasty, crystalline mass, and after recrystallisation from ether, the solid product melted at 56°, which is the melting point of dibenzylmethylsilicic oxide.

#### *Treatment of Silicic Oxides with the Grignard Reagents.*

As already stated, the oxides or ethers of the general formula  $(R_2Si)_2O$  seem to be unchanged by the Grignard reagents. Experiments were made with benzylethylpropylsilicic oxide and with tribenzylsilicic oxide, which were finally heated at about 200° during an hour with magnesium propyl bromide and magnesium ethyl bromide respectively; in both cases, as far as could be ascertained, the original substance was recovered unchanged.

#### *Tertiary Silicols from Substituted Metasilicic Acids.*

Benzylmetasilicic acid, prepared by decomposing benzylsilicon trichloride with cold water, was treated with a large excess of an ethereal solution of magnesium benzyl chloride, and after the ether had been distilled, the residue was heated slowly up to about 220°. The product was then cooled, treated with water, and submitted to steam distillation until free from dibenzyl. The pasty mass which then remained was separated with the aid of ether and distilled under diminished pressure (20 mm.). The fraction collected from about 250° to 300° quickly solidified, and when crystallised from a mixture of chloroform and light petroleum yielded a pure sample of tribenzylsilicol. The yield was not good (only 5 grams of the pure silicol from 14 grams of the acid), and a large proportion of the crude product, probably unchanged acid, did not distil below 360°/20 mm.

Phenylmetasilicic acid, prepared from phenylsilicon trichloride, was treated with a large excess of magnesium phenyl bromide, and after the mixture had been heated to about 220°, the product of the reaction was separated from diphenyl and submitted to distillation. The fraction collected from about 270° to 300°/14 mm.,

solidified when cooled, and consisted almost entirely of triphenylsilicic acid; about 5 grams of the pure silicol were obtained from 10 grams of the acid.

*Phenylmetasilicic Acid.*

This compound was prepared long ago by Ladenburg by the hydrolysis of phenylsilicon trichloride with dilute ammonium hydroxide solution. The substance thus obtained is, when dried, a transparent, vitreous, brittle solid, and is readily soluble in ether and many other organic liquids, as well as in a solution of potassium hydroxide.

When phenylsilicon trichloride is hydrolysed with cold water, or even when it is poured into hot water, it gives a product having the above properties, but under certain conditions a very different result is obtained. This observation was made in the course of some experiments on the preparation of diphenylsilicon dichloride and by the interaction of silicon tetrachloride, bromobenzene, and magnesium in presence of ether. Some fractions of low boiling point resulting from this preparation, and consisting of a mixture of bromobenzene and phenylsilicon trichloride, were directly treated with steam in order to remove the bromobenzene and obtain phenylmetasilicic acid. Instead of an oily residue of phenylmetasilicic acid, a white, brittle solid remained.

In order to ascertain the nature of this product, some pure phenylsilicon trichloride was prepared and directly treated with steam; it was rapidly transformed into a white solid, which was separated and repeatedly extracted with ether in order to free it from phenylmetasilicic acid, but very little (about 1 per cent.) of this substance was obtained. As the residue was insoluble in all the many organic liquids which were tried, it was dried at 120° and analysed; two different preparations gave the following results:

0·3308 gave 0·1536 SiO<sub>2</sub>. Si=21·8.

0·3344 „ 0·1546 SiO<sub>2</sub>. Si=21·7.

0·1700 „ 0·3460 CO<sub>2</sub> and 0·0596 H<sub>2</sub>O. C=55·5; H=3·9.

(C<sub>6</sub>H<sub>5</sub>SiO)<sub>2</sub>O requires Si=21·9; C=55·6; H=3·9 per cent.

In making the combustion, the substance was previously mixed with copper oxide, as great difficulty was experienced in the silicon estimations in getting rid of the whole of the carbon.

The method of formation of this solid and the analytical results show that it is the anhydride of phenylmetasilicic acid. It is slowly acted on by a concentrated solution of aqueous alcoholic potash, and apparently is converted into a potassium salt of phenylmetasilicic acid; benzene is not formed in appreciable quantities, and after the alcohol is expelled, the solution gives with mineral acids after

some time a precipitate which resembles phenylmetasilic acid in all its properties.

Although the anhydride is so readily formed from phenylsilicon trichloride, it is not readily produced when the acid is heated at 100°; a sample of the acid which had been heated during many hours still dissolved readily in ether.

The authors gratefully acknowledge the financial assistance for which they are indebted to the Government Grant Committee of the Royal Society.

UNIVERSITY COLLEGE,  
NOTTINGHAM.

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XIX.—*Intramolecular Rearrangements of Diphenylmethane *o*-Sulphoxide.*

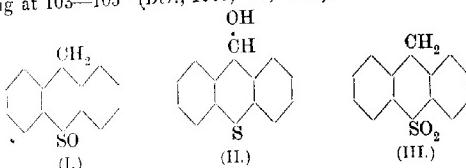
By THOMAS PERCY HILDITCH and SAMUEL SMILES.

THE changes which the ortho-sulphoxides of diphenylamine suffer on treatment with acid reagents (*Trans.*, 1909, **95**, 1253; 1910, **97**, 186, 1112, 1559) demonstrate the instability of the thionyl group and the tendency of sulphur at that stage of oxidation to revert to the bivalent state through the intermediate phase of the sulphonium arrangement. Further illustration of this property of the thionyl group has been found in the simpler hydroxy-aromatic sulphoxides (*Trans.*, 1910, **97**, 2248), which are converted into halogen derivatives of the sulphides on being heated with halogen acids. With these substances the intermediate sulphonium derivatives are more difficult to detect, chiefly on account of their inferior stability; but in experiments which are now being conducted some definite evidence of their existence has been obtained.

In extending this inquiry, we have first turned our attention to the behaviour of diphenylmethane *o*-sulphoxide (**I**), and, on account of the close structural resemblance between this substance and the corresponding derivative of diphenylamine, it was anticipated that a comparison of the behaviour of the two series would yield information on the mechanism of the reaction beyond that already obtained.

In order to obtain this sulphoxide, thiophanthen was oxidised with hydrogen dioxide in acetic anhydride solution, in accordance with the method which has been found suitable for the oxidation of thio- to thionyl compounds. The product melted at 109°, and gave analytical data corresponding with the required substance; but the

isomeric thioxanthenol (II) has recently been obtained by F. Mayer from the reduction of thioxanthone, and it is described by him as melting at 103—105° (*Ber.*, 1909, **42**, 1134).



It therefore appeared possible that the products of the two reactions, namely, the oxidation of thioxanthen and the reduction of thioxanthone, might be identical, and since no direct proof of the constitution of the substance obtained by reducing thioxanthone has ever been given, it became necessary more completely to demonstrate the constitution of the two substances.

*Constitution of Thioxanthenol and of Diphenylmethane o-Sulphoxide.*

That the products from the two sources are evidently different is shown by the melting point of a mixture of approximately equal quantities; it is indefinite, and lies in the neighbourhood of 75—80°. The structure of thioxanthenol formed by reduction of thioxanthone is shown by the following facts:

(i) It is converted into thioxanthone by oxidation with the calculated amount of potassium permanganate in cold glacial acetic acid.

(ii) It yields a benzoyl derivative when treated with benzoyl chloride in pyridine solution.

(iii) It reacts with phenylcarbimide; the product, however, appears to be unstable, decomposing into diphenyl carbamide.

Further, it is clear that the product melting at 109°, which is formed by oxidising thioxanthen with hydrogen dioxide under the conditions described in the experimental part of this paper, is the required diphenylmethane *o*-sulphoxide (II), for

(i) It yields diphenylmethane *o*-sulphone (III) when treated with the calculated amount of potassium permanganate in cold glacial acetic acid.

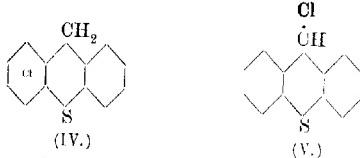
(ii) It does not react with phenylcarbimide, nor does it yield a benzoyl or acetyl derivative with the usual reagents.

*The Action of Acids on Thioxanthenol.*

The action of acid reagents on thioxanthenol has been mentioned by Werner (*Ber.*, 1901, **34**, 3311) at the conclusion of his study

of the carboxonium salts. Werner found that solutions of thioxanthenol became coloured by the addition of mineral acids, and when bromine vapour was passed into the solution of thioxanthenol in aqueous hydrogen bromide, he obtained a crystalline perbromide; but since no analytical data was given, we have repeated and extended these experiments. The carbothionium chloride (VI) is obtained as a brick-red, crystalline precipitate when an ethereal solution of thioxanthenol is saturated with hydrogen chloride. This substance is not sufficiently stable to be obtained in a condition suitable for analysis, but it yields a stable, red, double salt with ferric chloride. Werner (*loc. cit.*) has pointed out that xanthenol may be regarded as the pseudo-base of the carboxonium salts, and that the same relation probably holds between thioxanthenol and the carbothionium salts, and we find, in accordance with this view, that the red salt is reconverted into thioxanthenol by the action of alkaline reagents.

At the same time, we have succeeded in obtaining an intermediate substance in this change; when the carbothionium chloride is dried in a vacuous desiccator to remove excess of hydrogen chloride, it is converted into an isomeric colourless substance for which there are two alternative structures available, namely, those of the chlorothioxanthen (IV) and the thioxanthenyl chloride (V):



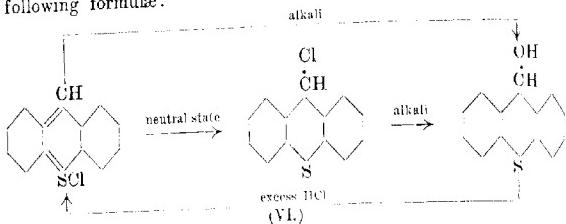
The former substance might be expected to be formed in accordance with the reaction which takes place between phenazothionium chloride and excess of hydrogen chloride (Trans., 1910, 97, 1112) when chlorothiodiphenylamine is formed; but this structure for the substance now in question cannot be accepted, for the halogen is very easily removed by alkaline reagents or even by water, thioxanthenol being formed. The compound must therefore be regarded as the carbonium chloride.

The change effected on thus passing from the sulphonium to the carbonium chloride involves the removal of halogen from quadrivalent sulphur to carbon; and in the light of other work and the migration of halogen in aromatic compounds, especially that of Orton on the transformation of *N*-chloroacetylarylamines (*Proc. Roy. Soc.*, 1902, 71, 156), it appears probable that the reaction takes place by the addition and subsequent removal of hydrogen chloride.

Moreover, this view of the process is confirmed by the recent vol. XCIX.

experiments of Gomberg and Cone (*Annalen*, 1910, **376**, 183), who find that the salts\* obtained by the action of halogen acids on phenylthioxanthenol contain an additional molecule of halogen acid which is lost in the transformation to the carbonium halide.

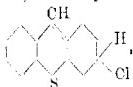
The conditions under which the reverse change of thioxanthenyl chloride into thioxanthonium salt takes place have not been clearly ascertained, but, so far as our experiments have been carried, it seems the mere presence of excess of acid is sufficient. The relations which hold between this group of substances are indicated by the following formulæ:



#### *Conversion of Diphenylmethane o-Sulphoxide into Thioxanthonium.*

Like thioxanthenol, the ortho-sulphoxide of diphenylmethane is converted by mineral acids into the thioxanthonium salts, but the speed with which this transformation takes place is less than in the former instance. This sulphoxide, however, cannot be regarded as the pseudo-base of thioxanthonium, for, as previously mentioned, thioxanthenol is formed by the action of alkaline reagents on the latter substance. At the same time, it is clear that by the successive application of the acid and alkaline reagents the diphenylmethane o-sulphoxide may be converted into thioxanthenol, the net result

\* It is necessary to mention that Gomberg and Cone (*Annalen*, 1909, **370**, 142; 1910, **376**, 183) on account of certain analogies to triphenylcarbinol have recently advocated a quinocarbonium structure, for example,



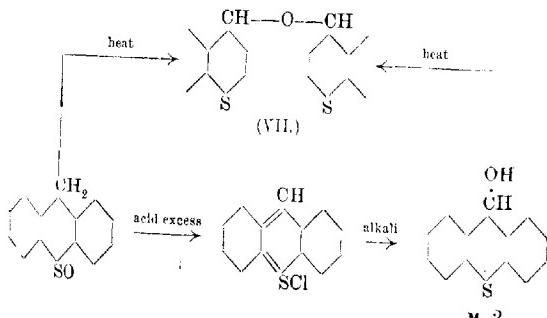
for these coloured salts as well as for those of the corresponding acridonium, xanthonium and azothionium series. We prefer, however, to retain the azo-oxium, thio-oxium, and oxonium structures which have been advocated for these substances by Hewitt (*Zeitsch. physikal. Chem.*, 1900, **34**, 9), Kehrmann (*Annalen*, 1902, **322**, 1), Werner (*Ber.*, 1901, **34**, 3300) and others. Both Kehrmann (*Annalen*, 1910, **372**, 287) and Hewitt and Thole (*Proc.*, 1910, **26**, 225) have recently opposed the view of Gomberg and Cone, and, so far as the thio-compounds are concerned, the present authors have yet other reasons for disagreement with the quinocarbonium structure, but the publication of this is deferred until the experiments from these other sources have been completed.

of the change being the transference of oxygen from sulphur to carbon. It is interesting to find that this transference may be effected by the aid of heat alone.

Thioxanthenol behaves under the influence of heat like its congener, xanthenol (R. Meyer, *Ber.*, 1896, **29**, 1276), for, when heated alone or in glacial acetic acid to about 120°, it furnishes the thioxanthenyl oxide (VII); and the same substance is formed when diphenylmethane *o*-sulphoxide is treated in a similar manner, the sole difference being that the yields are somewhat smaller, and more prolonged heating is required. Further evidence of this change may be adduced from the behaviour of thioxanthen with hydrogen dioxide in glacial acetic acid solution. If the boiling solution of this substance is mixed with excess of hydrogen dioxide good yields of diphenylmethane *o*-sulphone are obtained. On the other hand, if a cold solution of thioxanthen in acetic acid containing about one molecular proportion of the oxidising agent is heated gradually to the boiling point, the chief product is thioxanthone. Evidently the latter circumstance is due to the conversion of the sulphoxide, which is slowly formed by the dilute peroxide into thioxanthenol, the latter in turn being oxidised to thioxanthone. Under the first set of conditions, the large excess of peroxide completes the oxidation of the thionyl group before the change to thioxanthenol has proceeded to any appreciable extent.

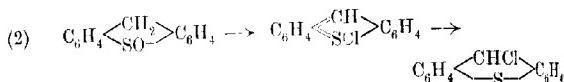
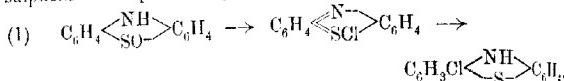
Moreover, it may be remarked that the mixture of sulphoxide and thioxanthenol, which melts indefinitely at 75–80°, if heated for a short time to about 110° and then allowed to cool and solidify, melts on re-heating at a much higher temperature in the neighbourhood of 100–102°. So far as we are aware, diphenylmethane *o*-sulphoxide is the only substance of that class which melts at a lower temperature than the corresponding sulphide, and it is possible that the anomaly is due to this isomerising action of heat.

The following formulae summarise the relations which connect these substances:

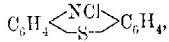


The probable mechanism of the conversion of the sulphoxide to the thioxanthonium salt is discussed in a subsequent paragraph.

Regarding the relations between these derivatives of thiadiphenylmethane from a general point of view, it is evident that they are closely parallel to those which have been previously observed (Trans., 1909, **95**, 1253; 1910, **97**, 186, 1112, 1559) with the thiadiphenylamine group, for in each series the quadrivalent sulphur of the thionyl group is reduced by the prolonged action of halogen acid to the bivalent state through the intermediate stage of an unsaturated sulphonium arrangement. Moreover, the same terminal stage has been observed with the simpler aromatic hydroxysulphoxides, and it is hoped that here, too, the intermediate sulphonium compound may be isolated:



There is, however, an interesting difference between the final products obtained in the two series, for in the thiadiphenylamine group the halogen finally enters the aromatic nucleus, whereas in the thiadiphenylmethane series it does not, but instead remains attached to the methane carbon atom. Armstrong (Trans., 1900, **77**, 1051), Orton (Trans., 1909, **95**, 14), and others have shown how easily the *N*-chloro-derivatives of acylarylamines are transformed into the aromatic halides by the intervention of free hydrogen chloride; and in view of the isolation of this carbonium chloride in the diphenylmethane series, it appears not improbable that the corresponding *N*-chloro-compound:

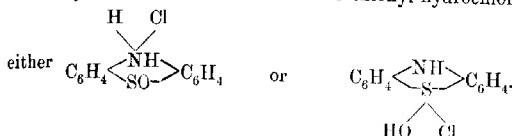


has a transitory existence during the action of hydrogen chloride on the phenazothionium salt.

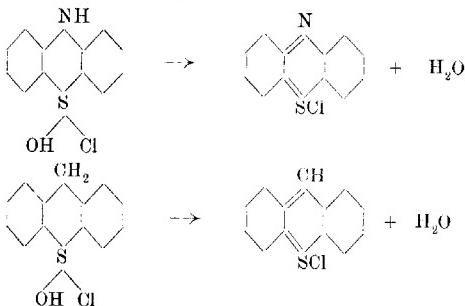
Turning to consider the mechanism by which these sulphoxide are converted into the corresponding azo- or carbo-thionium salts the permissible assumption is made that in the two series the processes are alike in their essential features, although perhaps minor differences may arise from the more pronounced basic power of the thiadiphenylamine compounds.

Investigation of the latter group has shown (Barnett and Smiles Trans., 1910, **97**, 186) that the reaction does not consist of the

mere transference of hydrogen from the amino- to the thionyl group, but that it depends on the preliminary formation of a salt. The subsequent observation (Brady and Smiles, Trans., 1910, **97**, 1559) that the monohydrochloride of trichlorothiodiphenylamine sulphoxide is very easily converted—merely by warming in certain solvents—into the azothonium compound indicates that it is only the mono-acid salt which is essential, but it was difficult to decide with certainty whether this is the amine or thionyl hydrochloride:



When, however, it is considered that the *o*-sulphoxide of diphenylmethane contains only one group of basic function, it becomes clear that not only is the formation of a mono-acid salt sufficient, but that this essential must be the sulphoxide salt. Finally, on regarding the structures of these substances:



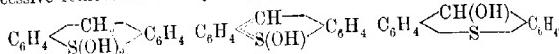
It is seen that the simplest way in which the formation of the cation salts can take place is by the elimination of water, and we consider that this conception of the process affords a satisfactory explanation of every case of this transformation which has hitherto been studied.

Without entering into the details of each case in particular, it may be sufficient to discuss one example which is of an exceptional nature. Of all the nitro-derivatives of diphenylamine *o*-sulphoxide, the tetranitro-compound is the most difficult to convert into the azothonium form by the action of mineral acids, but it is the only one of them which is transformed by the action of heat. This substance is also exceptional in containing an additional molecular proportion of water, which is only removed with great difficulty,

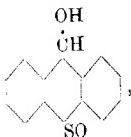
and thus weight is given to the suspicion that the thionyl group may here exist in the ortho-condition,  $>\text{S}(\text{OH})_2$ .

The exceptional behaviour of this substance is thus readily explained, for a thionyl compound which is capable of separate existence in this form would, according to the hypothesis now advanced, be more readily converted by heat into the azothionium compound than one which is incapable.

Evidence for the existence of the thionyl group in this ortho-form has elsewhere been given by one of the present authors (*Trans., 1906, 89, 697*) and by others (for example, Fromm and Raiziss, *Annalen, 1910, 374, 90*), and there can be no doubt that the salts which that group forms with acids are derived from that structure. On regarding the diphenylmethane *o*-sulphoxide from this point of view, it is seen that the somewhat complex transformation into thioxanthonium and thence into thioxanthenal is merely the successive removal of two hydroxyl groups from the thionyl group:

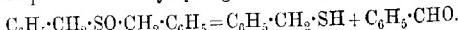


In order to ascertain whether this process can be continued until the methane carbon atom is saturated with oxygen, we have examined diphenylcarbinol *o*-sulphoxide:

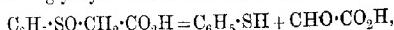


hoping to obtain thioxanthone from it by similar reactions. However, we have not been able to effect this rearrangement under the usual conditions.

In conclusion, it may be remarked that this transference of oxygen from thionyl to methylene in the thiadiphenylmethane series is not an isolated occurrence of that reaction, for a similar behaviour has been observed with open-chain compounds in which these groups are adjacent. Smythe (*Trans., 1909, 93, 349*), for example, has noticed the formation of benzaldehyde and benzyl mercaptan from benzyl sulphoxide and dry hydrogen chloride:

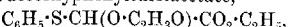


Also, Pummerer (*Ber., 1909, 42, 2202*) has met with a similar behaviour in phenylsulphoxyacetic acid, which yields phenyl mercaptan and glyoxylic acid under the influence of mineral acids:



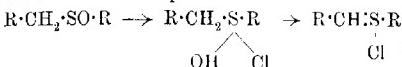
but he found that with the ester of this acid (*Ber., 1910, 43, 1401*)

the rearrangement may be carried out without rupture of the molecule, ethyl  $\alpha$ -acetoxyphenylthiolacetate,



being obtained by the action of acetic anhydride.

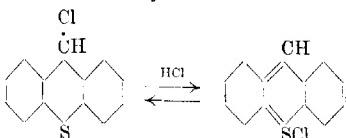
Pummerer has advocated the hypothesis (*Ber.*, 409, **42**, 2282; see also Fromm and Erfurt, *ibid.*, 3812) that these sulphoxides, containing the group  $\cdot\text{CH}_2\cdot\text{SO}\cdot$ , may owe their instability in presence of acids to a tendency to form an unsaturated sulphonium base which undergoes the observed decomposition:



Although no experimental evidence was advanced directly to support this conclusion, there can be little doubt in the light of the present experiments that it is correct. Pummerer, however, and apparently also Fromm (Fromm and Raiziss, *Annalen*, 1910, **374**, 90), seem to regard the sulphonium hydroxide and the methylene-sulphoxide as tautomeric. To justify this conclusion, it is necessary to isolate these unsaturated fatty sulphonium bases, and, if ever this be successful, we consider it very doubtful whether the hypothesis of tautomerism will be borne out, for the experiment with the ester of phenylsulphoxyacetic acid seems to point to the conversion of the sulphonium hydroxide into the hydroxy-acid.

At any rate, in the thiadiphenylmethane series there can be no question of tautomerism between the diphenylmethane *o*-sulphoxide and the carbothionium hydroxide, for the latter, when liberated from its salts with alkali, gives thioxanthenol and, so far as we are aware, not even a small quantity of the sulphoxide.

It appears, however, that in certain solvents an equilibrium between the thioxanthenyl chloride and carbothionium salt may be established by means of free hydrochloric acid:



or if excess of acid be added, the latter salt is formed, whilst if the acid be removed (see also Gomberg and Cone, *Annalen*, 1910, **176**, 183) the carbonium chloride is obtained.

#### EXPERIMENTAL.

The chief difficulty in the way of these experiments was the preparation of thioxanthen in sufficiently large quantities; but this

has been met by the convenient synthesis of that substance from *o*-thiolbenzoic acid and benzene in presence of sulphuric acid (Davis and Smiles, Trans., 1910, **97**, 1290). Thioxanthone was then reduced to thioxanthen by Graebe and Schulthess's method (*Annalen*, 1891, **263**, 1), which consists in heating with phosphorus and hydriodic acid in sealed tubes. A specimen of the thioxanthen, which was employed in the following experiments, melted, after being recrystallised from light petroleum, at 128–129°, and gave the requisite analytical data. (Found, C=79·1; H=5·2. Calc., C=78·8; H=5·0 per cent.)

*Oxidation of Thioxanthen.*

(a) *With Hydrogen Dioxide in Acetic Anhydride:* Diphenylmethane *o*-Sulphoxide,  $C_6H_4\begin{array}{l} < \\ \text{CH}_2 \\ > \\ \text{SO} \end{array}C_6H_4$ .—A solution of thioxanthen in acetic anhydride was gradually mixed with about twice the quantity of aqueous hydrogen dioxide necessary for complete conversion into sulphoxide. The mixture was then set aside at the atmospheric temperature, being shaken at frequent intervals. After the lapse of a short time the temperature increased, but this was not allowed to rise above 35°, the reaction being checked by immersing the vessel in melting ice. If the mixture was kept at about 30°, the reaction proceeded quietly, and was soon complete. When no further rise of temperature was observed after removing the vessel from the cooling-bath, the mixture was poured on powdered ice. When the pale yellow, crystalline precipitate had completely separated, it was collected and recrystallised from light petroleum, in which it is sparingly soluble, and *diphenylmethane o-sulphoxide* was obtained in soft flakes, melting at 109–110°:

0·1325 gave 0·3561 CO<sub>2</sub> and 0·0489 H<sub>2</sub>O. C=73·28; H=4·10.

0·1214 „ 0·3240 CO<sub>2</sub> „ 0·0462 H<sub>2</sub>O. C=72·78; H=4·2.

$C_{18}H_{10}OS$  requires C=72·90; H=4·6 per cent.

The compound is insoluble in water, and sparingly so in ether. When dry ferric chloride is added to a solution in the latter medium, a double salt is precipitated in fine, yellow needles. This behaviour has been observed with other aromatic sulphoxides (Hofmann and Ott, *Ber.*, 1907, **40**, 4930), and appears to be characteristic. The action of heat and acids on this sulphoxide is described later.

In the preparation of this substance, it is important to prevent the temperature rising above the limit mentioned, otherwise the reaction is apt to get out of control, and when this occurs the product is almost entirely diphenylmethane *o*-sulphone (m. p.

168–169°). Also, it is advisable to employ only small quantities—about 5 grams—of thioxanthen.

(b) *With Potassium Permanganate in Acetone.*—The sulphoxide may also be prepared by a process similar to that applied to *N*-methylthiodiphenylamine (Barnett and Smiles, Trans., 1910, **97**, 188). The calculated amount of permanganate was added in small portions to a solution of thioxanthen in acetone, which was kept faintly acid with sulphuric acid during the reaction. After pouring the mixture into water, and removing any oxides of manganese by the addition of sulphurous acid, a quantity of the sulphoxide was obtained; but the yields were not good, the product being contaminated with sulphone.

(c) *With Hydrogen Dioxide in Acetic Acid:* *Diphenylmethane o-Sulphone*,  $\text{C}_6\text{H}_4\left<\text{CH}_2\right>\text{SO}_2\text{C}_6\text{H}_4$ , and *Thioxanthone*.—Excess of concentrated hydrogen dioxide was added to a boiling solution of thioxanthen in glacial acetic acid. The action proceeded vigorously, and the temperature was maintained at the boiling point for a few minutes.

On cooling the liquid, a quantity of diphenylmethane *o*-sulphone separated in colourless needles (m. p. 170°). (Found, C=67·8; H=4·2. Calc., C=67·8; H=4·3 per cent.) No other product was isolated from the reaction carried out under these conditions.

Other experiments were made in which approximately equimolecular proportions of hydrogen dioxide and thioxanthen were employed. In these experiments the peroxide was added to a cold dilute solution of thioxanthen in glacial acetic acid, the mixture being then slowly warmed to the boiling point. On cooling the contents of the flask, thioxanthone separated in the characteristic yellow needles. It melted at 209°, and was identified by a mixed melting-point determination.

The different course taken by the process of oxidation under these sets of conditions has been dealt with in the theoretical part of this paper.

#### *Constitution of Diphenylmethane o-Sulphoxide.*

(a) *Oxidation.*—Two grams of the sulphoxide were dissolved in cold glacial acetic acid, and an amount of potassium permanganate corresponding with one gram-atom of available oxygen for every gram-molecule of sulphoxide was gradually added. The reaction was assisted by shaking, and when it was complete the mixture was poured into cold water and then mixed with sulphurous acid. The colourless solid was collected, and finally crystallised from acetone. Diphenylmethane sulphone was thus obtained in small, colourless

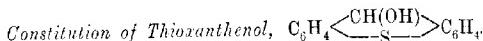
prisms, which melted at  $169^{\circ}$  (Graebe, *loc. cit.*, gives  $168^{\circ}$ , and Lapworth, *Trans.*, 1898, **73**, 408, gives  $169-170^{\circ}$ ). (Found, C = 67·61; H = 4·37. Calc., C = 67·82; H = 4·35 per cent.)

(b) *Behaviour with Phenylcarbimide.*—A solution of the sulphoxide in excess of phenylcarbimide was set aside at the atmospheric temperature for some days; after the lapse of that time a very few crystals of diphenylcarbamide had separated, otherwise no interaction could be detected (compare thioxanthenol, p. 157).

(c) *Behaviour with Benzoyl Chloride.*—A slight excess of benzoyl chloride was slowly added to a cooled solution of the sulphoxide in pyridine. After being kept at the atmospheric temperature for twenty-four hours, the mixture was poured into excess of dilute aqueous sulphuric acid. The oil which then separated quickly solidified. The product was recrystallised from light petroleum, from which it separated in the soft crystals characteristic of the sulphoxide.

These melted at  $109-110^{\circ}$ , whether alone or mixed with a sample of diphenylmethane *o*-sulphoxide. No other product could be isolated from this reaction. It is evident that, under the conditions given above, diphenylmethane *o*-sulphoxide does not react with benzoyl chloride (compare thioxanthenol, p. 157).

It may be remarked that a mixture of this sulphoxide with thioxanthenol melts at a lower temperature than either—at about  $70-75^{\circ}$  if nearly equal quantities be mixed.



We at first attempted the preparation of this substance by the method described by Werner (*Ber.*, 1901, **34**, 3310), who added zinc dust to thioxanthone, which was suspended in a boiling alcoholic solution of sodium ethoxide. The product obtained by this method, however, melted indefinitely at  $150-155^{\circ}$ , and appeared to be a mixture of at least two substances, and we therefore adopted the use of potassium ethoxide in place of sodium ethoxide, as recommended by F. Mayer (*Ber.*, 1909, **42**, 1132). The substance used in the following experiments melted, after being recrystallised from light petroleum, at  $103-104^{\circ}$ . (Found, C = 72·8; H = 4·66. Calc., C = 72·9; H = 4·67 per cent.)

The yield of the substance obtained by this method is not always good, and it varies considerably. So far as we have been able to ascertain, the yield is favoured by allowing the reduction to proceed vigorously, by excluding air from the vessel to prevent oxidation of the thioxanthenol, and by not allowing the temperature to rise too high on prolonging the reaction, otherwise thioxanthenyl oxide may be formed.

(a) Oxidation of thioxanthenol with potassium permanganate in glacial acetic acid was carried out in a manner precisely similar to that described with diphenylmethane *o*-sulphoxide.

The product crystallised from acetic acid in yellow needles, which melted at 209°, and possessed all the properties of thioxanthone. (Found, C=73·9; H=4·0. Calc., C=73·6; H=3·8 per cent.) The yield was good, and no other product was isolated.

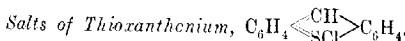
(b) Behaviour with Phenylcarbimide.—A solution of dry thioxanthenol in phenylcarbimide, when kept at the atmospheric temperature, quickly gave a copious deposit of a crystalline substance. After the lapse of a few days this was collected. It was apparently a mixture, but after being twice or thrice recrystallised from absolute alcohol, it furnished diphenylcarbamide (m. p. 236—238°).

It is difficult to say whether this is formed by a decomposition of a carbamate during crystallisation, or by the mere withdrawal of water from the thioxanthenol. In any case, the behaviour of thioxanthenol with phenylcarbimide is quite different from that of diphenylmethane *o*-sulphoxide.

(c) Benzoylation of thioxanthenol was effected in pyridine solution with benzoyl chloride. The treatment of the reaction mixture was the same as that applied in the case of diphenylmethane *o*-sulphoxide (p. 156). The product, benzoylthioxanthenol, was crystallised from alcohol, when it was obtained in leaflets of a pale yellow tint; these melted somewhat indefinitely at 124—128°:

0·1040 gave 0·2859 CO<sub>2</sub> and 0·0414 H<sub>2</sub>O. C=74·98; H=4·42.  
C<sub>20</sub>H<sub>14</sub>O<sub>3</sub>S requires C=75·48; H=4·4 per cent.

The interaction of acetyl chloride and thioxanthenol in pyridine solution furnished thioxanthenyl oxide (see p. 159), and the same substance was obtained by interaction with hot acetic anhydride. Thioxanthenol is further clearly distinguished from the diphenylmethane *o*-sulphoxide by the interaction with ferric chloride. When this substance is added to an ethereal solution of thioxanthenol, the red ferrichloride of thioxanthonium is obtained as a crystalline precipitate. The sulphoxide yields the normal yellow addition product.



(a) From Thioxanthenol.—Thioxanthenol dissolves in concentrated sulphuric acid or in alcoholic hydrogen chloride, giving deep red solutions of the corresponding salts of thioxanthonium. The sulphate may be obtained in the solid state by adding a drop of sulphuric acid to an ethereal solution of thioxanthenol.

*Thioxanthonium chloride* was prepared by saturating an ethereal solution of thioxanthenol with dry hydrogen chloride at 0°. The

liquid rapidly assumed a deep red colour, and, when completely saturated with the acid, it deposited a copious crystalline precipitate. Thioxanthonium chloride crystallises in brick-red needles with a metallic lustre. It is readily soluble in alcoholic hydrogen chloride, and sparingly so in ether which has been saturated with that acid. It is rapidly hydrolysed by water or solvents such as alcohol, giving thioxanthenol. Analysis of this chloride was not directly effected, for after the crystalline material had been collected and immediately placed over alkali in a vacuous desiccator on porous earthenware, it was rapidly transformed into the colourless thioxanthenyl chloride.

For analysis the substance was converted into the stable ferrichloride. This substance was obtained by adding an ethereal solution of anhydrous ferric chloride to the deep red solution obtained by saturating thioxanthenol in ether with hydrogen chloride.

When prepared in this manner, *thioxanthonium ferrichloride* forms bright red needles, which melt at 193–194°:

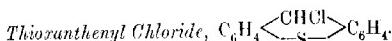
0·1313 gave 0·1889 CO<sub>2</sub> and 0·0287 H<sub>2</sub>O. C=39·23; H=2·43.

0·1747 „ 0·0355 Fe<sub>2</sub>O<sub>3</sub>. Fe=14·22.

C<sub>13</sub>H<sub>9</sub>ClS, FeCl<sub>3</sub> requires C=39·5; H=2·28; Fe=14·18 per cent.

(b) *From Diphenylmethane o-Sulphoxide.*—The solution of this sulphoxide in concentrated sulphuric acid has the same appearance as that of thioxanthenol, and on adding water to it the latter substance is precipitated.

The action of alcoholic hydrogen chloride on the sulphoxide is slower than with thioxanthenol, but the red solution of thioxanthonium chloride is finally produced. The best method of preparing the chloride in the solid condition from the sulphoxide is to work in ethereal solution as with thioxanthenol. The product was identified by conversion to the ferrichloride mentioned in the foregoing paragraph. The crystalline sample obtained melted at 190°. (Found, C=39·66; H=2·8; Fe=14·20. Calc., C=39·50; H=2·28; Fe=14·18 per cent.)



When the solid thioxanthonium chloride is kept in a vacuous desiccator over solid alkali hydroxide to remove excess of acid, the red crystals of the substance rapidly break up and lose their colour, the mass finally becoming almost colourless. Analysis was conducted with a sample which had been dried in this manner:

0·1203 gave 0·2973 CO<sub>2</sub> and 0·0421 H<sub>2</sub>O. C=67·47; H=3·89.

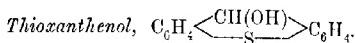
C<sub>13</sub>H<sub>9</sub>ClS requires C=67·11; H=3·87 per cent.

Reasons for assuming the carbonium structure for this substance have been given in a foregoing paragraph.

Thioxanthenyl chloride is soluble in ether, and melts at 112–113°; there is no doubt that in the pure condition the substance is colourless, the pale colour of these samples obtained being due to traces of enclosed thioxanthonium salt. The substance was not recrystallised on account of the extreme ease with which it is hydrolysed. Evidence of this hydrolysis is furnished by estimations of chlorine at intervals after preparation, the sample remaining over calcium chloride in a desiccator which was frequently opened:

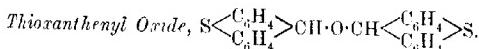
After one day, Cl=13·68; after three days, Cl=12·33; after five days, Cl=10·51.

$C_{13}H_9ClS$  requires Cl=15·27 per cent.



(a) *From Thioxanthenyl Chloride.*—Two experiments were performed; in one the chloride was saturated with water, and in the other with dilute alkali hydroxide. The solid material was extracted with ether, and finally crystallised from light petroleum. In each case thioxanthenol and thioxanthone were obtained; these were identified by their melting points, alone and mixed with other samples of these substances. There is no doubt that the latter substance is formed by oxidation of thioxanthenol by atmospheric oxygen.

(b) *From Thioxanthonium Salts.*—The various salts of thioxanthonium, for example, sulphate and chloride, are readily converted into thioxanthenol by excess of water. An experiment was also made with the ferrichloride, of which the details are given. The salt was triitated with cold aqueous alkali hydroxide, and the precipitate which then formed was collected, dried, and extracted with alcohol. The solution deposited thioxanthenol, melting at 103–105°. (Found, C=72·6; H=5·0. Calc., C=72·9; H=4·6 per cent.)



(a) *From Thioxanthenol.*—A few grams of this substance were heated in a bath at 120°. After the lapse of about one hour, the material had resolidified to a dark-coloured, crystalline cake. This was recrystallised from boiling glacial acetic acid, when thioxanthenyl oxide was obtained in pale yellow needles, which melted at 314–315°;

0·1401 gave 0·3918 CO<sub>2</sub> and 0·0558 H<sub>2</sub>O. C=76·25; H=4·43.

C<sub>20</sub>H<sub>18</sub>OS<sub>2</sub> requires C=76·08; H=4·39 per cent.

The substance is very sparingly soluble in cold glacial acetic acid, and is decomposed by mineral acids, giving red solutions of thioxanthonium salts.

From the mother liquors of this preparation thioxanthone was isolated (m. p. 208°; C=73·4; H=4·5. Calc., C=73·5; H=3·7 per cent.), being formed by oxidation of the thioxanthenol by atmospheric oxygen.

It was later found that thioxanthenyl oxide is formed in better yield and in a purer condition by boiling a solution of thioxanthenol in glacial acetic acid. The substance is rapidly deposited from the boiling solution in the crystalline state.

(b) *From Diphenylmethane o-Sulphoxide.*—The method employed was the same as that described with thioxanthenol, except that the heating was continued for a longer period. The yields of thioxanthenyl oxide was not so good as in the former case, and the substance was not so easily obtained in the pure condition. The sample obtained by recrystallisation of the product melted at 310°. (Found, C=76·38; H=4·48. Calc., C=76·08; H=4·39 per cent.)

As with thioxanthenol, much better yields are obtained by boiling the sulphoxide in glacial acetic acid; the oxide is then precipitated from the cooled liquid in an almost pure condition (m. p. 314—315°; C=76·05; H=4·8. Calc., C=76·08; H=4·39 per cent.).

When experiments were made with other boiling solvents, it appeared that the transformation of the sulphoxide depends not only on the temperature of ebullition, but on the nature of the liquid. For example, a solution of the sulphoxide in pyridine was boiled (115°) for some hours, but almost the whole of the sulphoxide employed was recovered (m. p. 109°; C=73·1; H=4·9. Calc., C=72·9; H=4·6 per cent.).

In conclusion, we desire to express our thanks to the Research Fund Committee of the Society for a grant which has partly defrayed the cost of these experiments.

THE ORGANIC CHEMISTRY LABORATORY,  
UNIVERSITY COLLEGE, LONDON.

XX.—*o-Carboxyanilides of the Sugars.*

By JAMES COLQUHOUN IRVINE and ALEXANDER HYND, M.A., B.Sc.  
(Carnegie Scholar).

In papers recently published from this laboratory it has been shown (Trans., 1908, **93**, 1429; 1909, **95**, 1545) that the condensation of reducing sugars with amino-compounds may take place in two distinct ways, according as the sugar reacts as an aldehyde or as a  $\gamma$ -oxide. One of the compounds discussed in this connexion was glucose-*o*-carboxyanilide, the reactions of which indicate that the linking of the sugar residue with anthranilic acid takes place through nitrogen. As this result bears directly on the general question of the formation of sugar complexes containing nitrogen, we have examined the behaviour of other sugars towards anthranilic acid, and have succeeded in preparing compounds analogous to glucose-*o*-carboxyanilide from galactose, rhamnose, mannose, and maltose. Condensation also proceeded in the case of fructose, but no definite compound was isolated, whilst lactose did not react. This negative result is in itself significant, as lactose is probably the only reducing sugar which forms a true aldehyde-ammonia compound.

The condensation proceeded easily in dilute alcoholic solution in the cold; all the compounds were found to react as acids, and the coupling of the anthranilic acid therefore takes place through the amino-group. In other respects, also, the carboxyanilides resemble the corresponding anilides closely, but are more unstable, so that it is impossible to confirm their structure by the methylation process (*loc. cit.*). In the following table it is shown that in each case the compounds display mutarotation which is strictly comparable with that undergone by the corresponding unsubstituted anilides and by the methylated anilides, for which the  $\gamma$ -oxidic structure has already been established.

*Mutarotation of Anilides and Substituted Anilides.*

	Glucose.	Galactose.	Mannose.	Rhamnose.	Maltose.
Anilide .....	+10° → -52°	-87° → -7°	-172° → -82°	+137° → +77°	
Methylated anilide .....	+221° → +47°	-17° → +35°	-98° → -39°	+133° → +7°	-
$\alpha$ -Anilide .....	+87° → -14°	-17° → +4°	-29° → -21°	-149° → -100°	+40° → +68°
$\beta$ -Anilide .....	-145° instead of +145°				

\* In Trans., 1909, **95**, 1555, the permanent value for this compound is given as +145° instead of -145°.

As the mutarotation of the carboxyanilides is exceedingly rapid,  
no special significance may be attached to the magnitudes of the

initial specific rotations, but it will be seen that the three derivatives of each sugar show mutarotation of the same order, and it would thus appear that all the above compounds are similarly constituted. It should be stated that it was only with the greatest difficulty that the above optical changes were observed, as the solutions generally attained equilibrium in a few minutes, and this suggests that other sugar complexes, at present regarded as existing in one form only, may possibly be composed of interconvertible forms.

Condensation, similar to that described, seems also to take place between sugars and certain aliphatic amino-acids, as we have succeeded in condensing glucose with  $\alpha$ -aminopropionic acid. The product of the reaction, glucoscalanide, does not display normal mutarotation, but the compound behaves in a curious manner when heated in aqueous solution. The optical activity then diminished from  $[\alpha]_D^{25} +45.7^\circ$  to the constant value  $24.6^\circ$ , and it was only on subsequent treatment with dilute acid that the specific rotation increased to that calculated on the assumption that one molecular proportion of glucose had been formed on hydrolysis. This result may be explained in various ways. The diminution first observed may be due to the establishment of an equilibrium between  $\alpha$ - and  $\beta$ -forms of a glucosidic glucoscalanide, and the subsequent rise in rotatory power to normal hydrolysis into the constituents. An equally valid explanation would be that the substance under examination was a mixture of stereoisomeric forms, which was partly hydrolysed by water and completely hydrolysed by acids. Such a mixture might contain *d*-glucose-*d*-alanide and *d*-glucose-*l*-alanide, or  $\alpha$ -glucose-*r*-alanide and  $\beta$ -glucose-*r*-alanide. In all probability, the compound is a mixture of the  $\alpha$ - and  $\beta$ -forms which are interconvertible in the neighbourhood of  $100^\circ$ . The instability of the substance prevented further work on this question and the sparing solubility of aliphatic amino-acids in dilute alcohol proved an obstacle in attempts to prepare other examples of this type of compound.

As a convenient method of gaining an insight into the structure of sugar derivatives is to study the corresponding alkylated compounds, we have attempted to prepare a series of condensation products from tetramethyl glucose analogons to those described in this paper and in previous publications. Unexpected difficulties were, however, encountered, in that, although unsubstituted sugars are much less reactive than alkylated sugars so far as condensation with hydroxy-compounds is concerned, the reverse holds true when the union of the condensed residues takes place through nitrogen. It seems therefore that the use of alkylated sugars in this connexion will prove of limited application.

We find that tetramethyl glucose does not give a definite condensation compound with anthranilic acid, or with alanine, and, when heated in alcoholic solution with *p*-phenetidine,  $\beta$ -naphthylamine, or with semicarbazide, the reaction does not proceed so smoothly as in the case of glucose. A well-defined *p*-toluidide was, however, obtained, which reacted like a glucoside towards silver oxide and methyl iodide, and showed extensive mutarotation. In sharp contrast to glucose, the alkylated sugar was not affected by ammonia or by hydrogen cyanide in the cold. Reaction proceeded in each case at higher temperatures, but in the latter instance resulted in the formation of ammonium tetramethylglucoheptone.

Incidentally, we have made a further examination of tetramethyl glucoseoxime, with the object of ascertaining if the compound shows mutarotation. In previous work (Trans., 1908, **93**, 100) no indication of this change could be detected, although the structure assigned to the compound, on the evidence afforded by alkylation, would obviously involve the existence of two interconvertible forms. We have now succeeded in obtaining, by crystallisation, one form of the oxime giving the change  $[\alpha]_D^{25} + 23^\circ \rightarrow 30^\circ$  in methyl-alcoholic solution, and, as in previous cases, the reverse optical change ( $36^\circ \rightarrow 30^\circ$ ) was shown by the compound after fusion. The analogy between the methylated and unmethylated oximes is thus complete.

#### EXPERIMENTAL.

##### *Galactose-o-carboxyanilide.*

Ten grams of galactose (1 mol.) were boiled with 200 c.c. of alcohol (80 per cent.) until the sugar had passed into solution; 15 grams (2 mols.) of anthranilic acid were added, and the liquid cooled. After seventy hours, the rotation had diminished to the constant value  $[\alpha]_D + 17^\circ$ . The bulk of the alcohol was then removed under diminished pressure, the product separating from the concentrated solution in aggregates of small needles. The united crops were washed with dry ether and dried in a vacuum. Yield, 60 per cent.

The compound proved to be too unstable to permit of purification in bulk by recrystallisation. The only method of purification possible was to boil the substance for a considerable time with carefully purified ether, and afterwards to crystallise rapidly from ethyl alcohol. The use of more than two grams of material in the crystallisation resulted, even on spontaneous evaporation of the solvent, in the separation of some free sugar. The compound contains one molecule of combined water, which was only completely

removed by heating to 90°/15 mm. for several hours. Analysis of the dry residue gave:

Found, C=52·50; H=5·72; N=4·68.

$C_{18}H_{17}O_7N$  requires C=52·17; H=5·68; N=4·68 per cent.

The high carbon value found is probably due to the presence of a trace of free anthranilic acid, as the analytical figures were improved after heating the substance with a little alcohol.

The compound reacts feebly acid to litmus, and contains the carboxyl group, as a definite barium salt was obtained by neutralising a solution in 50 per cent. alcohol with barium hydroxide and precipitating with excess of alcohol. The barium content found for the dry product (Ba=19·6 per cent.) excludes the possibility of this precipitate being either barium *o*-aminobenzoate or barium galactosate, and shows the salt to be the *barium* derivative of galactose-*o*-carboxyanilide ( $C_{20}H_{32}O_{14}N_2Ba$ ).

As the mutarotatory changes shown by the carboxyanilide are complete in a few minutes, only small concentrations may be employed, in order to limit, so far as possible, the time interval which must elapse between contact of the solvent and the first observed rotation. The initial values found thus showed considerable variation, but the permanent values were quite uniform.

*Solvent: Ethyl alcohol. c = 1·1580. Mutarotation,  $[\alpha]_D^{20} - 17\cdot3^\circ \rightarrow +4\cdot3^\circ$*

The compound thus exists in two interconvertible forms, and judging from the results of a polarimetric study of the condensation carried out as described in previous papers, the levo-form is the first to be produced, and is formed almost immediately.

#### *Mannose-*o*-carboxyanilide.*

When an alcoholic solution of mannose is boiled with anthranilic acid, partial decomposition of the acid results, and no definite product seems to be formed. The method of slow condensation in the cold proved more successful. Ten grams of the sugar (1 mol.) were dissolved in 100 c.c. of alcohol (80 per cent.), and allowed to attain constant rotation; 15 grams (2 mols.) of anthranilic acid were then added, and the solution kept at the temperature of the room. After twenty-four hours, a colourless, gelatinous precipitate separated. This was removed by filtration, and the mother liquor put aside for three months. In this way the condensation product was obtained, in nearly quantitative amount, as long, colourless needles.

The compound was easily purified by recrystallisation from absolute ethyl alcohol, separating in small needles, melting at 126°,

from an 8 per cent. solution, and as a jelly from more concentrated solutions. Analysis showed the presence of one molecule of water:

Found, C=49·26; H=6·02; N=4·51.

$C_{13}H_{17}O_7N \cdot H_2O$  requires C=49·21; H=5·99; N=4·41 per cent.

Solvent: Methyl alcohol. c=2·041. Mutarotation,  $[\alpha]_D^{20} - 29\cdot4^\circ \rightarrow - 21\cdot1^\circ$ .

### Rhamnose-o-carboxyanilide.

On dissolving two molecular proportions of anthranilic acid in a 10 per cent. solution of hydrated rhamnose in 75 per cent. alcohol, a rapid fall in the dextrorotation resulted, and, after eight hours, an abundant crop of crystalline product separated. The mother liquor was worked up as in other cases, and yielded additional crops, the total yield being nearly quantitative. After purification from methyl alcohol, the compound was obtained in fine needles, melting at 167–168°. Although prepared in aqueous alcohol, and from hydrated rhamnose, the compound was anhydrous:

Found, C=55·20; H=6·26; N=4·95.

$C_{13}H_{17}O_6N$  requires C=55·08; H=6·06; N=4·94 per cent.

Rhamnose-o-carboxyanilide displays the usual solubilities and properties of these condensation compounds, but is characterised by unusually rapid mutarotation. The change is, in fact, not detectable in ethyl or methyl alcohol five minutes after the first contact of solvent and solute. Low concentrations were therefore used, and the initial values have little significance. The change is, however, much slower in pure pyridine, but even then is complete in twenty minutes:

Solvent.	Initial $[\alpha]_D^{20}$ .	Final $[\alpha]_D^{20}$ .	Time required to establish equilibrium.
Methyl alcohol .....	+ 66·4°	51·2°	5 minutes
Ethyl      "        .....	42·9	42·9	less than 5 minutes
Pyridine ..... .....	148·8	100·2	20 minutes

### Maltose-o-carboxyanilide.

The formation of this compound takes place slowly in the cold. A 7·5 per cent. solution of equilibrium maltose in 60 per cent. alcohol was mixed with slightly more than one molecular proportion of anthranilic acid, and put aside for three months. The solvent was then removed in a vacuum desiccator, and the dry, crystalline residue extracted with pure ether. The substance was so easily decomposed by solvents that it could not be further purified, but the melting point (153–155°) and microscopic examination showed the preparation to be uniform. When dried until constant in weight at 60°/15 mm., the compound contained one molecule of combined water:

Found, C=47·62; H=6·07; N=2·75.

$C_{19}H_{27}O_{12}N_2H_2O$  requires C=47·60; H=6·05; N=2·92 per cent.

The mutarotation was, for this type of compound, comparatively slow.

*Solvent:* Methyl alcohol.  $c=0\cdot9195$ . *Mutarotation*,  $[\alpha]_D^{20^\circ} + 48\cdot9^\circ \rightarrow 68\cdot0^\circ$ .

#### *Glucosalanide.*

Owing to the insolubility of alanine in alcohol, and also to the instability of the product, the preparation of this compound presented considerable difficulty. The condensation may, however, be carried out in dilute alcoholic solution either at the boiling point or in the cold, but only in the latter case can the product be obtained in the crystalline state.

A 3·5 per cent. solution of equilibrium glucose in methyl alcohol was kept at the boiling point under a condenser, and slightly more than one molecular proportion of alanine added. The acid was dissolved in water ( $\epsilon=10$ ), and the solution introduced drop by drop from a side-tube, which was kept warm so as to avoid the formation of nuclei of the acid. The resulting solution was finally boiled for eight hours, the specific rotation, calculated on the sugar used, diminishing in this time from  $+53^\circ$  to  $32^\circ$ . The solvent was removed in a vacuum, the residue dried at  $100^\circ$ , extracted with methyl alcohol, and precipitated with ether. The product was an amorphous powder, which deliquesced in air, and could not be obtained crystalline:

Found, C=43·64; H=6·82.

$C_9H_{17}O_7N$  requires C=43·03; H=6·77 per cent.

A better result was obtained by the method of slow condensation in the cold, the solution of sugar and acid being prepared as already described. After ten weeks the liquid was filtered from a trace of alanine which had separated, and evaporated in the usual manner. The residue consisted of delicate non-deliquescent needles, which softened at  $110^\circ$ , and melted without decomposing at  $114^\circ$ . No crystallising medium could be found, all attempts at purification resulting in decomposition:

Found, C=42·70; H=6·87; N=5·75.

$C_9H_{17}O_7N$  requires C=43·03; H=6·77; N=5·58 per cent.

*Glucosalanide* is freely soluble in alcohol or water, but no mutarotation was detected in either solvent in the cold. When an aqueous solution of the compound is heated to  $90^\circ$ , optical change results, which are summarised below:

*Solvent:* Water.  $c=1\cdot001.$

Specific rotation (permanent at 20°).....	.....	+ 45.7°
" " after two hours at 90° .....	.....	+ 24.6°
" " after hydrolysis with dilute acid.....	.....	+ 39.3°

The latter value, when corrected for the weight of glucose formed on hydrolysis, gives  $[\alpha]_D$  55°, so that presumably this sugar is the only active product of the change. This result is discussed in the introduction.

#### *Nitrogen Derivatives from Tetramethyl Glucose.*

As a rule, no reaction takes place between tetramethyl glucose and amino-compounds in the cold, and, at higher temperatures, the condensation is generally incomplete. Owing to solubility considerations, the separation of the unaltered sugar is difficult. The *p*-phenetidine,  $\beta$ -naphthylamide, and semicarbazone proved to be syrups, and, as the compounds were prepared by standard methods and no examination for mutarotation was possible, detailed description is unnecessary.

*Action of Ammonia.*—A 5 per cent. solution of the sugar in dry ether was saturated in the cold with dry ammonia, and after two days the solvent was removed in a vacuum. The product consisted entirely of unaltered sugar, and a duplicate experiment, in which methyl alcohol was used as solvent, also gave a negative result in the cold. On heating the latter solution at 90°, it was found that the activity diminished and became constant ( $[\alpha]_D + 43^\circ$ ) after twenty-five hours' treatment. The solvent was removed in a vacuum, and the residual syrup extracted in the cold with light petroleum. The extract contained an oil the reactions of which corresponded with those of a condensation product, but the analytical figures obtained were not sufficiently accurate to distinguish between the aldehyde-ammonia compound and tetramethyl glucoseimine.

*Action of Hydrogen Cyanide.*—Both ethereal and alcoholic solutions of the sugar remained unaltered in rotation when saturated with dry hydrogen cyanide and kept for several days. Experiments showed, however, that in methyl-alcoholic solution, reaction took place slowly at 90°, but after twenty hours' treatment the solution became too dark in colour to admit of further polarimetric readings. The solvent and hydrogen cyanide were removed in a vacuum, and the unaltered sugar extracted with boiling petroleum. The undissolved crystalline residue gave the reactions of an ammonium salt, and the methoxyl content found was  $OMe = 40.47$  per cent. This

result is in itself sufficient to show that the condensation is accompanied by hydrolysis, and that the compound described above is the ammonium salt of tetramethylglucoheptonic acid (Calc., OMe = 41·47 per cent.).

*Tetramethyl Glucose-p-toluidide.*—This compound was prepared exactly as in the case of the corresponding anilide (*loc. cit.*), heating being continued for two hours, after which the solvent and excess of the base were removed in a vacuum. The product crystallised in long prisms from light petroleum, and melted at 144°:

Found, C = 62·46; H = 8·10; OMe = 37·7.

$C_{17}H_{27}O_5N$  requires C = 62·70; H = 8·37; OMe = 38·1 per cent.

Unlike the unmethylated toluidide, the compound shows no tendency to exist in hydrated forms, and thus the examination for mutarotation was unattended by complications.

*Solvent: Methyl alcohol.* c = 1·093. *Mutarotation*,  $[\alpha]_D^{20} + 156\cdot5^\circ \rightarrow 53\cdot5^\circ$ .

The compound was recovered unaltered after prolonged heating with a large excess of silver oxide and methyl iodide, and is thus a  $\gamma$ -oxide. (Found, OMe = 38·8 per cent.)

*Tetramethyl Glucosoxime.*—The alkylated oxime was prepared as already described (*loc. cit.*), and recrystallised several times from a mixture, in equal parts, of dry ether and low-boiling petroleum. No mutarotation was detected so long as the melting point was below 70°, but rapid crystallisation showed a continual rise in melting point until the maximum of 88° was reached. This preparation showed slight mutarotation.

*Solvent: Methyl alcohol.* c = 1·50. *Mutarotation*,  $[\alpha]_D^{20} + 23\cdot3^\circ \rightarrow 29\cdot97^\circ$ .

After fusion for one hour at 100°, the same specimen, similarly dissolved, showed the reverse change:  $[\alpha]_D^{20} + 36\cdot4^\circ \rightarrow 30\cdot0^\circ$ .

The authors gratefully acknowledge the receipt of a research grant from the Carnegie Trust in aid of the above investigation.

CHEMICAL RESEARCH LABORATORY,  
UNITED COLLEGE OF ST. SALVATOR AND ST. LEONARD,  
UNIVERSITY OF ST. ANDREWS.

XXI.—*Cupritartrates and Analogous Compounds.*

By SPENCER UMFREVILLE PICKERING, M.A., F.R.S.

*Tartrates.*

$\beta$ -Cupritartrate No. 1.—When potassium or sodium hydroxide is added to copper tartrate, the amount required to produce alkalinity is, according to Kahlenberg (*Zeitsch. physikal. Chem.*, 1895, 17, 586), and also according to Masson and Steele (*Trans.*, 1899, 75, 725), 1·25 to 1·27 KOH for each atom of copper. The present author obtained similar values with ordinary "pure" potassium hydroxide, but on using sodium hydroxide carefully prepared from the metal, and a well-boiled solution of copper tartrate (which is soluble to the extent of 0·015 per cent. of copper), the value obtained was 1·34NaOH (variation from 1·36 to 1·32). Phenolphthalein was used as indicator.

The product of the reaction is a deep blue solution, which, on the addition of the excess of alkali, becomes violet-blue, constituting then Fehling's solution. According to Masson and Steele, when alcohol is added to the neutral liquid, a crystalline substance separates out in the case of the sodium compound, but its composition could not be determined, owing to its decomposition on drying. The corresponding potassium compound suffers no such decomposition, but it separates as a dark blue, gummy mass: on washing this with alcohol, and drying at 100°, a very dark blue, brittle, scaly substance was obtained, to which Masson and Steele attribute the formula  $K_3C_{12}H_7Cu_3O_{18} \cdot 5H_2O$ . No explanation, however, was attempted of its constitution, although they showed that it contained copper in the electronegative portion of the molecule, and that potassium tartrate was one of the products of the reaction yielding it.

It is legitimate to question the purity of a substance obtained as a gummy mass, and it was found that with certain precautions it could be thrown down as a rather light blue precipitate, which, however, proved to be an emulsion; this could be collected, dissolved in water, and re-precipitated. After the first precipitation, no difficulty was experienced in obtaining it in the emulsion form, but the emulsion became finer at each precipitation, and the operation could not be repeated more than five or six times.

Two samples of the substance purified in this way gave the following values:

A.	Found : Cu=30·36	K=12·76 per cent.	Ratio=3:2·05
B.	" Cu=31·24	K=12·69 "	" =3:1·98
Cal.	: Cu=31·01	K=12·72 "	" =3:2·00

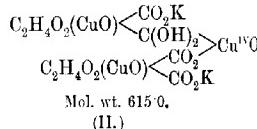
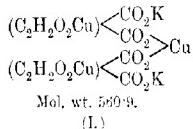
Samples less thoroughly purified contained excess of potassium, due, no doubt, to the presence of potassium tartrate, with ratios for Cu: K from 3: 2·18 down to those quoted above, but in no case was a ratio found as high as that obtained by Masson and Steele (3: 2·25).

The copper and potassium were determined, as in the case of the cupricitrates, by igniting the compound, determining the copper as oxide, and the potassium as carbonate. As the substance "scatters" on ignition, it was first decomposed by heating at a low temperature in a large closed tube, then washed into a platinum basin, evaporated, and ignited more strongly. Traces of copper always adhered obstinately to the dish, and some also passed through the filter: these were estimated separately.

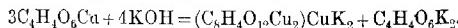
A solution of the substance may be evaporated very easily, and, unlike the cupricitrates, it rapidly attains a constant weight at 100°. On heating to a higher temperature, even to 110—115°, it begins to decompose, and leaves a residue of copper oxide on dissolution.

A solution evaporated until solidification begins, and left to stand, forms eventually a clear blue glass (obtained also by Masson and Steele), which contains about 9H<sub>2</sub>O: after many months this glass becomes slightly cloudy, owing to the separation of cuprous oxide. Occasionally the substance has been obtained on evaporation in small quantities in feathery crystals, and a few crystals are also deposited sometimes on the sides of the vessel from the solution to which alcohol has been added. The dried substance, when exposed to the air, spits in all directions, particles of it being projected to a distance of 12 or 18 inches.

The molecular proportion, copper: potassium = 3: 2 agrees with that in a potassium cupritartrate with copper displacing the hydrogen atoms in the alcoholic hydroxyl groups (I); it also agrees



exactly with the proportion of alkali which was found necessary to produce alkalinity, according to the equation:



The molecular weight, however, of such a compound is 560·9, whereas the minimum molecular weight deduced—taking the ratio Cu: K = 3: 2—from the percentage of copper found is 619·1, and from the potassium 614·6, mean 616·8. Such a value agrees within

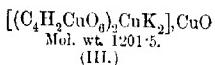
experimental error with formula II, which represents all the copper as entering the molecule by the addition of CuO, instead of the metal displacing an equivalent of hydrogen. The CuO group on the right is represented as in the cupricrates, with quadrivalent copper; the nature and method of connexion of the other CuO groups will be discussed below.

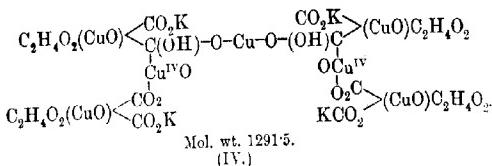
*β Cupritartrate No. 2.*—When to a solution of the above cupritartrate, potassium hydroxide is added in the proportion of one molecule, or more, to each atom of copper present, and the liquid heated, it soon becomes opaque, through the separation of much cuprous and cupric oxide in a very fine state of division. If the proportion of alkali added is less than 0·3 KOH, the liquid remains clear on heating, but yellow flakes of cuprous oxide separate, many of which float on the surface of the liquid. With an intermediate proportion, however, namely, 0·3 to 0·7 KOH, no cuprous oxide is formed, but the liquid, on heating, becomes deeper in colour, and a blue, gelatinous precipitate gradually separates, the whole becoming semi-solid. If alcohol, insufficient to cause precipitation, is added to the alkaline cupritartrate before heating, then, when heat is applied, the same substance is thrown down in a flocculent condition. The precipitate in either case was found to be decomposed by washing with water, and was, therefore, freed from adherent liquid by pressure in very thin layers between tiles. On drying at 100° it soon attained a constant weight, and then consisted of a violet-blue powder. On raising the temperature, slight blackening began at 110°, with a loss in weight corresponding with less than 1H<sub>2</sub>O on the formula given below. Two samples, *A* and *B*, prepared without alcohol, and two prepared with it, *C* and *D*, gave:

*A.	Found : Cu=33·92	K=12·70 per cent.	Ratio = 7:1·26
B.	Cu=34·77	K=12·62	" = 7:1·13
C.	Cu=35·04	K=12·25	" = 7:3·98
D.	Cu=34·54	K=12·61	" = 7:1·15
Mean :	Cu=34·57	K=12·54	" = 7:1·13
Calc. :	Cu=34·46	K=12·11	" = 7:1·00

\* Results less certain, owing to smallness of sample.

The values for potassium would probably be high, owing to the impossibility of washing the substance; taking, therefore, the molecular ratio as being 7:4, the compound may be represented on the alcoholic hydroxyl theory by the formula III, or on the views suggested by the results with the cupritartrate No. 1, and with the cupricrates, by the formula IV, which depicts it as a derivative from two molecules of the first cupritartrate by the substitution of an atom of copper for two of the hydroxylic hydrogen atoms:





The molecular weight deduced from the copper percentage is 1287, which agrees well with the formula IV, but is 86 units higher than that required by formula III.

The formation of this substance from No. 1 by the action of potassium hydroxide involves the formation at the same time of some other cupritartrate, similar to those described by Bullnheimer and Seitz (see below).

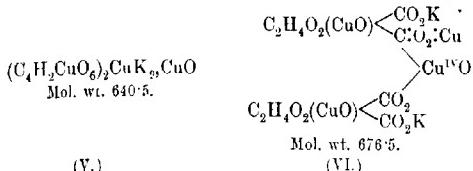
*β-Cupritartrate No. 3.*—When the last-mentioned compound is separated from the liquid from which it has been precipitated, and shaken with a large volume of water, it is decomposed, much copper passing into solution, and a denser violet-blue solid being left. This, in its turn, is decomposed by water, but only very gradually, the wash-water, when it is washed by decantation throughout many days, containing continuously about 0·002 per cent. of copper, after which it falls to faint traces or to nil, and the precipitate is then found to have been deprived entirely of its potassium.

The first product of the action of water, when dried at 100°, yields a violet-blue substance, which is so dark as to appear almost black before it is ground. It attains a constant weight rapidly, and loses very little further weight at 115°, when a darkening indicates that decomposition is beginning. Two samples, prepared from different preparations of No. 2, by washing until the copper contents of the filtrate became constant, gave the results A and B below. In the case of C, some of No. 2 was dried before being washed, and then washed on a filter with a little water, which seemed to remove at once the bulk of the soluble copper. In D some of the liquid containing the precipitated compound No. 2 was heated on a water-bath for three hours, and the residue collected and washed:

A.	Found : Cu=37·47	K=10·76 per cent.	Ratio = 4:1·87
B.	" Cu=37·13	K=10·53 "	" = 4:1·84
C.	" Cu=37·18	K=11·47 "	" = 4:2·00
D.	" Cu=37·44	K= 9·38 "	" = 4:1·71
	Mean : Cu=37·31	K=10·68 "	" = 4:1·88
	Calc. : Cu=37·39	K=11·56 "	" = 4:2·00

This compound being, as mentioned above, deprived eventually of its potassium by water, the proportion of potassium formed would naturally be low, and the most probable ratio of copper : potassium is 4:2, which is actually attained in the sample C, when the action

of water was most restricted. Such a ratio would be given by formula VI below, representing a cupritartrate with both the carboxylic hydrogen atoms displaced by copper, and the calculated molecular weight agrees fairly well with that deduced from the percentage of copper, this giving 676·5, against 682, whereas an analogous compound represented according to the alcoholic hydroxyl theory, formula V, would require a molecular weight of only 640·5:



The relationship between the three cupritartrates is very simple, one molecule of No. 2 splitting up into molecules of Nos. 1 and 3.

*Other Cupritartrates.*—When the cupritartrate No. 3 is washed continuously by decantation with successive additions of water until the liquid no longer contains any potassium, two different substances are obtained according to circumstances; one of these is quite insoluble in water, is blue on drying at 100°, and gave, as a mean, Cu=43·49, H<sub>2</sub>O (lost at 155°)=6·23 per cent., values which agree with those for an ordinary basic salt, C<sub>4</sub>H<sub>4</sub>O<sub>6</sub>Cu.Cu(OH)<sub>2</sub>, namely, Cu=43·51, H<sub>2</sub>O=6·17 per cent. The other dissolved sufficiently in water to give a faint reaction with ferrocyanide, was of a violet-blue colour, and gave, as a mean, Cu=48·42 per cent., which agrees with the copper in a compound of a formula similar to VI above, with an atom of that metal displacing the two potassium atoms, namely, 48·02 per cent.

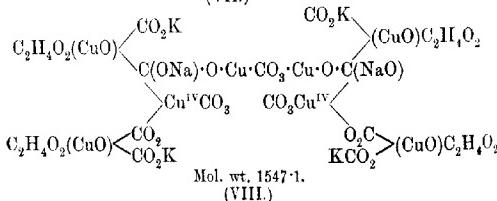
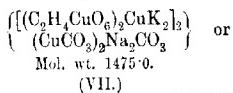
Bulinheimer and Seitz (*Ber.*, 1899, **32**, 2347; 1900, **33**, 817) obtained several tartrates and racemates which they represent on the alcoholic hydroxyl theory by the formula (C<sub>4</sub>H<sub>2</sub>CuO<sub>6</sub>)M'<sub>2</sub> for the single salts, and (C<sub>4</sub>H<sub>2</sub>CuO<sub>6</sub>)M'<sub>2</sub>(C<sub>4</sub>H<sub>2</sub>M'<sub>2</sub>O<sub>6</sub>)M'<sub>2</sub> for the double salts. These formed deeply coloured crystals, were insoluble in alcohol, and dissolved in water, giving a strongly alkaline reaction. Unfortunately the alkalinity was not determined, and its existence is inconsistent with the single salts being represented by the above formula. These salts, also, in such cases as were examined, retained one molecule of water which could not be driven off without decomposition, and which is probably constitutional water. The compounds would appear to be analogous to Luff's cupricitrate, and it is proposed to examine them in order to ascertain whether the formula suggested in that case (*Trans.*, 1910, **97**, 1844) will apply to them also.

*α-Cupritartrate*.—The composition of potassium α-cupriticrate corresponded with that of a substance consisting of two potassium cupricrate nuclei united by a molecule of potassio-cupric carbonate; such a view received further support from the fact that potassio cupric carbonate, although decomposed by water into a basic salt, dissolves freely in even a weak solution of potassium cupricrate (Trans., 1910, **97**, 1845). Some carbon dioxide is given off during dissolution, owing to the simultaneous formation of another cupricrate. A solution of potassium cupritartrate was also found to dissolve the double carbonate, but in that case no carbon dioxide was evolved.

Various circumstances appeared to complicate the results in the case of potassium cupricarbonate, which was not so in the case of the analogous sodium compound, and this salt therefore was used. Excess of it was shaken up for some time with a strong solution of potassium cupritartrate No. 1; the quantity remaining undissolved was determined by filtering, and decomposing the residue with water. It was found that rather more than twice as much of the double carbonate had dissolved as was required by the above-mentioned proportions. To the strong solution, without any of the washings from the undissolved residue, alcohol was added, and this precipitated all the copper present in the form of a light blue substance, which appeared to be partly solid and partly emulsion. The alcoholic liquid was found to be alkaline, and contained about half (Found, 53 per cent.) of the sodium carbonate in the sodio-cupric carbonate which had passed into solution; hence the carbonates must have become combined with the cupritartrate in the proportion of  $2\text{CuCO}_3 : \text{Na}_2\text{CO}_3$ . Analysis of the substance confirmed this. After drying at  $100^\circ$ , two preparations gave the mean values:

Found: Cu=32·60      K=10·07      Na=2·96 per cent.      Ratio=8·02:2·01  
Calc.: Cu=32·87      K=10·11      Na=2·97      "      " =8·00:2·00

This may be represented by:



The molecular weight deduced from the copper percentage is 1560, and that from alkali metals is 1553, mean 1556, which agrees well with formula VIII. The formula VII, on the alcoholic hydroxyl theory, gives much too low a molecular weight, and, indeed, independent of this evidence against it, it is difficult to see how the constitution of such a substance can be explained on this theory at all. The alkalinity of the compound was found to correspond with the two atoms of sodium present.

When heated at 100° without previous drying, this substance appears to be partly melted and decomposed, but if dried previously over sulphuric acid, no such decomposition occurs. It then forms a light, violet-blue solid, which can be easily powdered. It begins to change in colour at 125°, and at 140° some carbon dioxide is evolved. From certain observations it seemed probable that other  $\alpha$ -cupritartrates, that is, cupritartrates containing carbonate, existed, especially when the carbonate used was that of potassium.

#### *Saccharates.*

**$\beta$ -Cuprisaccharate.**— Copper saccharate, prepared by double decomposition,\* and having the composition  $C_6H_8O_8Cu \cdot 2H_2O$  at 100°, requires 1.49KOH to become alkaline, indicating the formation of a compound analogous to the cupritartrate No. 3 (p. 173):



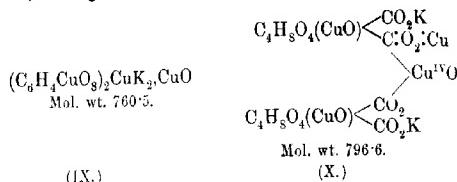
On adding alcohol to the blue solution thus obtained, a bulky, light blue precipitate was formed, which, when dried at 100°, appeared almost black, although it showed a violet-blue colour when ground. On dissolving it in water, and reprecipitating it, it became darker and more transparent at each precipitation, and finally it was so transparent that no precipitate could be recognised as present until the liquid was filtered.

Analyses of one preparation after four successive precipitations are given below (*A* to *D*), and indicate that excess of potassium hydroxide is present at first. In a second preparation a deficiency of alcohol was added for the first precipitation, and in that case the composition of the precipitate remained unaltered by repeated dissolution and precipitation (*E* and *F*), agreeing with that of the product ultimately obtained in the first preparation:

\* If a solution of it containing potassium sulphate is evaporated, a sulphosaccharate, which is freely soluble, is formed. Potassium hydroxide converts this into what is apparently a potassium cupri sulphosaccharate.

<i>A.</i>	Found : Cu = 25.27	K = 12.89 per cent.	Ratio = 4 : 3.32
<i>B.</i>	" Cu = 27.99	K = 12.46 "	" 4 : 2.89
<i>C.</i>	" Cu = 30.67	K = 10.59 "	" 4 : 2.24
<i>D.</i>	" Cu = 31.57	K = 10.08 "	" 4 : 2.08
<i>E.</i>	" Cu = 31.54	K = 10.02 "	" 4 : 2.06
<i>F.</i>	" Cu = 31.68	K = 10.07 "	" 4 : 2.07
	Mean : Cu = 31.60	K = 10.06 "	" 4 : 2.07
Theory	: Cu = 31.92	K = 9.82 "	" 4 : 2.00

The ratio of the potassium to copper is somewhat high, but leaves little doubt that it should be 2 : 4, as indicated by the amount of potassium hydroxide required for the formation of the substance. The copper leads to a molecular weight of 804·7, and the potassium to 777·3, the mean of which, 791, agrees fairly well with the formula X, analogous to that of the cupritartrate No. 3:



The temperature at which this salt was dried was 125°; when heated to a higher temperature decomposition begins, although with very little further loss in weight. On ignition, it swells up to a great bulk, but decomposes quietly. The anhydrous salt exhibits the same peculiarity as the  $\beta$ -cupritartrate No. 1, of scattering when exposed to air.

A weak solution of it gives no trace of red with ferrocyanide, however long it is kept, but if the solution is boiled, and then cooled before the ferrocyanide is added, a portion of the copper in it reacts, but only very slowly. After being kept in the cold for two days, the whole of the copper in the boiled solution again becomes inert. With a strong solution of the substance, ferrocyanide gives an almost black liquid, from which a brown precipitate separates after some hours.

### *Mucates.*

*β-Cuprimumate*.—Copper mucate, prepared by double decomposition, retains  $4\text{H}_2\text{O}$  at  $100^\circ$ , and becomes anhydrous at  $120^\circ$ . It dissolves in water to the extent of only 0·00008 per cent. of copper. When potassium hydroxide is added to it, it dissolves slowly to form a deep blue solution, the proportion required before alkalinity is reached being 1·59KOH for each atom of copper present, indicating a reaction similar to that occurring in the case of the saccharate. The solution obtained, unless very dilute, turns in a few minutes to a jelly; it is only when the copper percentage is

about 0·5, or less, that the solution, even when hot, can be filtered. It may be boiled without decomposition.

The addition of alcohol to it throws down a bulky, gelatinous precipitate, which, on re-dissolution in water and reprecipitation, becomes more transparent at each operation, as in the case of the cuprisaccharate. On drying, the precipitate forms a dark violet-blue powder, which suffers no decomposition until about 135°. The samples analysed were dried, therefore, at 120°. The results were similar to those with the cuprisaccharate; the ratio of Cu : K was as high as 4 : 3 or 4 : 2·5 after one precipitation, but fell and became constant after two or, sometimes, three precipitations. Two samples were also prepared without the addition of alcohol, by allowing the solution to gelatinise, and working the jelly on a tile until it was deprived of its moisture. The mean results with four specimens gave:

Found : Cu = 31·82	K = 9·61 per cent.	Ratio = 4 : 1·96
Calc. : Cu = 31·92	K = 9·82   ,,	,, = 4 : 2·00

The possible formulæ will be the same as those for the saccharate (p. 176), and the molecular weight calculated for the second of them, 796·6, agrees fairly well with that deduced from the above analyses, the copper giving 799·1, and the potassium, 813·7; mean, 806·4.

Potassium cuprimucate is a colloid, and its ready gelatinisation is in accordance with the known behaviour of colloids; but it exhibits a reversal of this change, which has not been noticed in other cases. When the jelly, which must not be too strong, is filtered under pressure, it passes completely through the paper, forming what appears to be a perfect solution, except that it is always slightly cloudy; this solution gelatinises again after a day or two. A similar change may be brought about by merely shaking the jelly, it being thereby converted into a solution. That the difference between the jelly and solution is not one in appearance only may be seen by placing some of each on a porous tile, when the solution is entirely absorbed, whilst the jelly is gradually deprived of its water, leaving a solid residue behind. As the jelly doubtless consists of aggregates of molecules, the change here noticed must be regarded as an instance of chemical combination, being broken down by such simple mechanical means as pressure or shock.

The cuprimucate, unlike the cuprisaccharate, always seems to react with ferrocyanide, but only very slowly.

#### *Cupriquinates.*

Although the compounds obtained from quinic acid have not afforded additional evidence as to molecular weight of these cupri-

compounds, they may be mentioned in connexion with those from the other tetrahydroxy-acids.

Copper quinate, prepared by boiling copper hydroxide or carbonate with quinic acid, and precipitating by alcohol, is a crystalline basic salt,  $[C_6H_7(OH)_4CO_2]_2Cu_2CuO$ , which contains  $8H_2O$  after drying at  $100^\circ$ , and dissolves in water to the extent of 0·02 per cent. of copper. Prolonged boiling of the acid with excess of carbonate results in the formation of a dark green, more highly basic quinate.

The addition of potassium hydroxide to copper quinate gives a solution which gelatinises after a few minutes, and cannot be filtered unless the copper content is less than 0·2 per cent. The cupriquinate thus resembles the cuprinucate, except as regards colour, and, also, that, when once it has been well boiled, it does not re-gelatinise. It seems impossible in this case to determine the exact point at which alkalinity appears on the addition of potassium hydroxide, the colour changes (with phenolphthalein as indicator) are uncertain, and the alkali required seems to vary with the dilution; various determinations gave from 0·67 to 1·0 KOH for each atom of copper. Excess of alkali gives a blue liquid. The precipitate obtained on adding alcohol to the neutral solution was also found to vary in composition, and likewise to vary rapidly in some cases when redissolved and reprecipitated. Two preparations thus treated and dried at  $125^\circ$ , which was the highest temperature which the substance would bear without decomposition, gave:

<i>A.</i>	1st Ppt. : Cu = 33·82	K = 9·45 per cent.	Ratio = 2 : 0·91
	2nd , , Cu = 35·16	K = 7·52, , ,	, , = 2 : 0·70
	3rd , , Cu = 36·63	K = 6·21 , , ,	, , = 2 : 0·55
<i>B.</i>	1st , , Cu = 34·94	K = 3·33 , , ,	, , = 2 : 0·16
	2nd , , Cu = 34·92	K = 3·25 , , ,	, , = 2 : 0·15
	3rd , , Cu = 31·99	K = 2·68 , , ,	, , = 2 : 0·10

The first preparation approached in composition to a potassium cupriquinate with two CuO groups,  $CO_2K \cdot C_6H_7(OH)_4 \cdot 2CuO$  (analogous to the cupritartrate, etc.), containing  $CuO = 32\cdot66$  and  $K = 10\cdot04$  per cent., the change on repeated precipitation consisting (as in the case of the cupritartrate) in the formation of some copper cupriquinate, which contains 41·71 per cent. CuO. The second preparation, however, is not amenable to such an explanation, and must contain some other cupri-compound.

Indefinite results of this character have, so far, been obtained in the case of several other monobasic acids which have been examined.

The cupriquinate requires the addition of a large volume of alcohol for its precipitation, and the precipitate, especially in the case of the second of the above preparations, was extraordinarily fine and transparent; the liquid remained quite clear and limpid, and passed through filter paper without leaving the slightest

residue; it was only when filtered through a Berkefeld filter that precipitation was found to have occurred, scarcely a trace of copper remaining in solution. When a solution of it is evaporated to a small bulk and left over sulphuric acid, it dries to a transparent, green, brittle glass, resembling the hydrated cupritartrate; after a time this becomes alkaline and opaque, copper oxide separating.

#### *Conclusion.*

The results detailed above can leave very little doubt that these cupri-compounds must be considered as substances in which CuO is added to the nucleus, and not as substances in which copper atoms displace hydrogen atoms, this applying to the hydrogen in the carboxyl groups, as well as to that in the alcoholic groups. The percentage errors between the found and calculated molecular weights on these two views are:

	Copper substituted for hydrogen.	CuO groups added to molecule.
$\beta$ -Cupitartrate	No. 1 .....	+ 10·0 per cent.
"	No. 2 .....	+ 7·0 "
"	No. 3 .....	+ 7·0 "
$\alpha$ -Cupitartrate.....	.....	+ 5·5 "
$\beta$ -Cupisaccharate .....	.....	+ 4·0 "
$\beta$ -Cupimucate.....	.....	+ 6·0 "

The difference between the two sets of formulae is in every case a question of the elements of water. With our imperfect knowledge of the nature of water of hydration, it is impossible to state confidently that water which cannot be eliminated without the decomposition of a substance is necessarily an integral part of the molecule, and, if we had to depend on an isolated instance, a determination of the molecular weight in such circumstances might be set aside; but when every one of the instances available bears the same evidence, this evidence cannot be ignored.

The nature of the CuO group in the carboxyl portion of the molecule has been discussed in previous communications, the copper being held to act as a tetrad; and it was originally suggested (Proc., 1910, 26, 17) that the CuO groups in the other portion of the molecule might be of a similar nature, with the copper atom united to two carbon atoms. Another view, which is, perhaps, less open to objection, is that the hydrogen atoms of the alcoholic hydroxyls become displaced by ( $\text{Cu}^{+2}\cdot\text{OH}$ )' groups. This was suggested many years ago to explain the constitution of substances formed by sucrose, mannitol and dulcitol with the oxides of copper, lead, barium and calcium, of which the molecular weights—as in the present instances—preclude their being represented as compounds derived from the substitution of hydrogen by the metal. Such a

view does not preclude the possibility of hydroxylic hydrogen being displaced by copper itself under other conditions; indeed, the only explanation of Luff's alkaline cupricitrate appears to depend on a partial substitution of that sort taking place as regards one hydrogen atom (see *Trans.*, 1910, **97**, 1844), added to which, there are compounds of sucrose with the alkali metals,  $C_{12}H_{21}M' O_{11}$ , apparently necessitating a similar substitution, although these compounds have not been investigated sufficiently for rigorous argument. There is, however, no evidence at present for believing that a copper atom ever displaces the two hydrogen atoms in two contiguous alcoholic groups, as represented in the hitherto accepted theory as to cupri-compounds.

HARPENDEN.

### XXII.—*The Reactions between Chemical Compounds and Living Muscle-Proteins.*

By VICTOR HERBERT VELEY.

EXPERIMENTS by Dr. Waller and the author on the comparative toxic effect of various classes of compounds on living muscle tissue have led to the conclusion that the results are due to chemical changes between the muscle-proteins (or their products of decomposition) and the compounds in the solutions of which the muscles are immersed (*Proc. Roy. Soc.*, 1909, *B*, **82**, 147; 1910, **82**, 206; *J. Physiol.*, 1910, **39**, 361; *Proc. physiol. Soc.*, 1908, 1909, 1910, etc.). These conclusions are based on the following arguments, stated briefly:

*Firstly*:—The temperature factors (namely, increase of rate of change per one degree absolute temperature) are practically identical with those previously observed for definite chemical changes; thus, the rate of increase per degree for the action of ethyl alcohol on muscle is almost identical with that of the reaction between hydrogen peroxide and hydrogen iodide (Harcourt and Esson), or of quinine with that between ferrous sulphate and chloric acid (Hood).

*Secondly*:—The relative reactivities of members of certain classes of compounds follow the same order (although often of a different degree of magnitude) as that observed in physico-chemical methods. Thus, the order of the paraffinoid alcohols is the same as that observed for their rates of esterification, and that of the halogen derivatives of acetic acid as their coefficients of affinity; or, again, the phenols are intermediate in their activity between the alcohols

and the carboxylic acids, precisely as the values of the heat effects of mixing equimolecular proportions of sodium hydroxide and the phenols are intermediate between those of the same base with the alcohols and carboxylic acids respectively. Examples might, of course, be multiplied.

*Thirdly:*—In certain cases there is evidence of a sub-division of the muscle stuff regarded as acidic and two bases, such as nicotine and quinine reacting simultaneously.

The object of the present communication is to carry the argument one step further, and to show that, in the absence of the disturbing factor of contracture, the reactions between living muscle stuff and chemical compounds can be made the subject of mathematical analysis. As the rate of reaction between *lifeless* chemical reagents is some function, generally logarithmic, and less generally linear, of time, so likewise the rate of reaction between *living* muscle stuff and a *lifeless* chemical compound follows the same general laws.

#### EXPERIMENTAL.

In order to make the subsequent text more intelligible, a description of the method of working, devised by Waller, is given in outline only. A sartorius muscle of a frog is dissected out and ligatured, with fine copper wires serving as conductors; the muscle is then set up in a glass vessel containing the solution (either 0·6 per cent. sodium chloride, approximately a *N*/10-solution, or that of the compound to be examined), and connected with a weighted lever recording its movements on a travelling smoked glass plate. The circuit with the secondary coil of an inductorium (Berne model) is completed on the one hand through the metal stand used to hold the glass vessel, and on the other by means of a direct wire; the primary coil is supplied by a 2-volt accumulator, and interrupted automatically every ten seconds by a clockwork relay. Independently there is also an electrically controlled clock for recording time in minutes by a lever on the same smoked plate.\*

When each induction shock is passed through the muscle, there is a response or kick, which moves the recording lever; if the solution possesses a toxic action, or, according to hypothesis, enters into chemical change with the muscle stuff, then these resulting responses decrease from a maximum to nothing as the time of operation increases.

For the purpose of measurement a photograph (same size) is taken of the record, and squared millimetre tissue paper placed thereon; a curve or line is drawn of the outline of the heights of the

\* In the actual experiments, parts of the apparatus, namely, vessel, muscle, and lever, were duplicated, so as to obtain simultaneous records.

responses, and of the base line or that of the lever; all irregularities due to the moment of inertia of the lever, as also those due to momentary defects of clockwork or otherwise, are thus eliminated. In other words, a smoothed curve or line is drawn.

If the heights in millimetres \* of the response be taken as the measure of the chemical change between the reacting substance and the muscle stuff, representing the number of potential units of chemical change, then a graph may be drawn with the heights of these responses as ordinates, and time, in minutes, as abscissæ. A graph of this type is given in a subsequent section.

*The Nature of the Chemical Changes.*—The investigations of Emil Fischer and his colleagues have shown that the final products of hydrolysis of the proteins are the amino-acids of the acetic series, and lactic acids, pyrrolidinecarboxylic acid, together with smaller quantities of other compounds of a similar type. Krimberg (*Zeitsch. physiol. Chem.*, 1907, **53**, 514) has obtained carnitine, the betaine of a hydroxybutyric acid, from muscle-protein.

The hypothesis can therefore be put forward that, when a muscle is immersed in the reacting solution, a partial hydrolysis of the proteins ensues, and the polypeptides thus formed subsequently react with acids, bases, or alcohols according to the equations given below, taken as simple illustrative types.

The completion of the changes, from left to right, is evidenced by an abolition of response, the formation of the products on the right-hand side producing a complete poisonous effect.

If the reacting solution be run out of the tube and saline solution substituted, then the chemical changes are reversed, and proceed from right to left, as shown by a recovery of the responses, at first small, and then subsequently increasing to their original height, less a difference due to the effect of fatigue, which will be separately discussed in the sequel.

The general equations are:

- (1)  $R(NH_2 \cdot OH)_x(CO_2 H)_y + xHA \rightleftharpoons R(NH_2 \cdot A)_x(CO_2 H)_y + xH_2 O$
- (2)  $R(NH_2 \cdot OH)_x(CO_2 H)_y + yBOH \rightleftharpoons R(NH_2 \cdot OH)_x(CO_2 B)_y + yH_2 O$
- (3)  $R(NH_2 \cdot OH)_x(CO_2 H)_y + yR'OH \rightleftharpoons R(NH_2 \cdot OH)_x(CO_2 R')_y + yH_2 O$

It will, of course, be understood that in the above equations the values of  $x$  and  $y$  are supposed to be quite unknown, and that the symbol  $R$  stands for a long and complicated chain of a polypeptide type. The equations are merely intended to indicate that the acid and basic groupings of the proteins or of, more probably,

\* These were measured by a graduated rule with sliding vernier; differences of 0.5 mm. being measured directly, intermediate differences taken as 0.3 mm. and 0.7 mm. as the case might be.

initial products of decomposition are the matters involved in the chemical change.

[The phenols probably behave as acids according to equation (1), rather than as alcohols according to equation (2).]

Another view which finds favour is that the products of hydrolysis are already present in the muscle stuff on account of its moribund condition, and are not formed as an intermediate chemical change.

The difference between this view or the one given above is, of course, one of degree and not of kind.

If there are two successive chemical changes, there would probably be an induction-period from a delay occasioned by the first change; in some cases such a delay was observed, but in others, not; so there is no balance of evidence in favour of either view.

However this may be, if the interpretation of the chemical changes is correct, then the amino-acids should produce little or no effect; results given in the sequel confirm this conclusion.

*The Rate of the Chemical Changes.*—It was observed in the introductory section that the rate of such changes between living muscle stuff and a chemical reagent, like those between two reagents, is generally a logarithmic, less generally a linear, function of time. These two cases are discussed in the succeeding sections.

(1) *Rate of Chemical Change a Logarithmic Function of Time.*—In many cases the rate of chemical change is in accordance with a reaction of the first order (unimolecular reaction), and expressible by a general equation:

$$K = \frac{1}{t} \log \frac{r_0}{r_t} . . . . . (1)$$

in which  $K$  = factor of chemical change,  $t$  = time,  $r_0$  = number of potential units of chemical change, or residue, when  $t=0$  and  $r_t$  = the same after time  $t$ .\*

This equation is realised in the following cases amongst others:

(1) *Maleic acid, N/200. Temperature 17°.*

The results are set out in the following table. In column I are given the times from start ( $t$ ); in column II, the number of units of potential chemical change or residue ( $r$ ), measured by the heights

\* This equation is more generally written  $K = \frac{1}{t} \log \frac{A}{A-x}$ , in which  $A=r_0$  and  $-x=r_t$ ; the above form appears preferable to the author, as the rate of any chemical change depends on the residue at any moment of time, although in many cases for the purpose of convenience measurements are made of  $A$ , the total amount of possible change, and  $x$ , a difference after a lapse of time  $t$ .

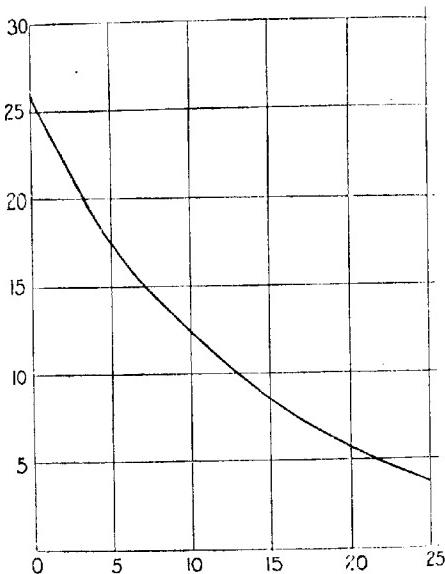
of responses; and in column III, the deduced values of  $K$ , or factor of chemical change.

(The same method will be adopted in succeeding tables without further explanation.)

TABLE I.

I.	II.	III.	I.	II.	III.
0	25.5	-	14	9.0	0.0306
.2	22.0	0.0277	16	8.0	0.0309
4	18.7	0.0315	18	7.0	0.0307
6	16.0	0.0323	20	6.0	0.0309
8	14.0	0.0314	22	5.3	0.0310
10	12.5	0.0301	24	4.5	0.0310
12	10.5	0.0314			

A graph is given in the figure, the values in column II being taken as ordinates, those in column I as abscissæ.



If the first result be omitted as a low value possibly due to some induction period, the mean value of  $K$  for the remainder is 0.0311, and in the succeeding table the values of the units of potential change calculated from this datum are compared with those observed.

TABLE II.

Time.	Units calc.	Units found.	Time.	Units calc.	Units found,
4	19.0	18.7	14	9.3	9.0
6	16.5	16.0	16	8.0	8.0
8	14.3	14.0	18	7.0	7.0
10	12.3	12.5	20	6.0	6.0
12	10.7	10.5	22	5.3	5.3
			24	4.5	4.5

The agreement between the two sets of numbers is within the limits of error in the method of measurement adopted.

For the sake of comparison, a set of observations by Cain and Nicoll (Trans., 1902, **81**, 1420) on the rate of decomposition of an aqueous solution of benzenediazonium chloride, as measured by the rate of evolution of nitrogen gas, is given in table III, being presented in the same form as that of table I.

TABLE III.

I.	II.	III.	I.	II.	III.
0	58.2	—	12	24.6	0.0312
6	38.9	0.0291	17	17.2	0.0310
8	32.8	0.0311	21	13.8	0.0306
10	25.3	0.0312	30	8.5	0.0287

The mean value of  $K$  in these observations is 0.0304, which only differs by about 2 per cent. from the figure 0.0311 given above, although the first set of observations relates to a reaction between maleic acid and muscle-protein, or its hydrolysis products, and the second to the decomposition of benzenediazonium chloride.

Apart from the element nitrogen in the one case belonging to an amino-group, and in the other to the allied diazo-grouping, there is nothing in common between the two sets of changes. It is therefore reasonable to suppose that the change, which occurs when a living muscle is immersed in a dilute aqueous solution of maleic acid, is of a *chemical* nature.

#### (2) Fumaric acid, N/200. Temperature 19°.

Observations with this acid were made mainly with a view of ascertaining whether geometrical isomerides would show any marked difference of behaviour. The results are given below; the values calculated from the mean value of  $K=0.01$  are given in column II(bis).

TABLE IV.

I.	II.	II(bis).	III.
0	17.0	—	—
2	11.0	10.7	0.094
4	6.5	6.7	0.102
6	4.2	4.3	0.101
8	2.5	2.7	0.104
10	1.6	1.5	0.094
12	1.2	1.0	0.100

The mean value of  $K$  for fumaric acid is rather more than three times than of maleic acid, which would show that the former is the more active of the two isomerides. This result is the opposite of that to be expected from physico-chemical measurements, such as electrical conductivity, rate of inversion of sucrose, etc., which give the higher value to maleic acid.

A repetition of the experiments under like conditions gave the same order for the two acids.

(3) *Acetic acid, N/200.*

The results obtained are given in table V, the calculated values in column II(bis) being calculated from a mean value of  $K=0.0355$ .

TABLE V.

I.	II.	II(bis).	III.	I.	II.	II(bis).	III.
0	17.0	—	—	14	5.5	5.7	0.0320
2	14.2	14.3	0.0340	16	5.0	4.8	0.0331
4	12.0	12.2	0.0353	18	4.2	4.0	0.0320
6	10.5	10.5	0.0334	20	3.8	3.5	0.0328
8	9.0	9.0	0.0345	22	3.2	3.0	0.0329
10	7.5	7.5	0.0351	24	2.7	2.7	0.0335
12	6.2	6.5	0.0348	26	2.3	2.5	0.0328

Although the degree of concordance is not of the fine order of accuracy to be expected in a study of a chemical reaction proceeding under fixed conditions and without disturbance of secondary changes, yet such concordance appears to be well within the limits of experimental error, having regard to the conditions of working.

(4) *Propionic acid, N/200.*

The results are given in the table below without further explanation. Mean value of  $K=0.0138$ .

TABLE VI.

I.	II.	II(bis).	III.	I.	II.	II(bis).	III.
0	15.0	—	—	12	10.0	10.2	0.0146
2	14.0	14.2	0.0150	14	9.5	9.5	0.0141
4	13.0	13.2	0.0155	16	9.0	9.0	0.0138
6	12.2	12.4	0.0153	18	8.5	8.5	0.0137
8	11.8	11.7	0.0130	20	8.0	8.0	0.0139
10	11.0	11.0	0.0124	—	—	—	—

In this series of results the first three observations give rather low values for heights of response, and consequently too high values of  $K$ .

As would be expected, acetic is stronger or more effective than propionic acid, the ratio of the  $K$  values being 355:138, or approximately 2.5:1. In physico-chemical methods, the ratio of

the two acids is approximately 1·3: 1, or otherwise the position of the two acids in physiological and physical methods is the same generally, but the relative order of magnitude different.

The results obtained with formic and butyric acids were identical with those of acetic acid within the limits of experimental error, although measurements by other methods have always led to a slightly higher value for the first-named.

#### *Basic Substances.*

*Leucine Hydrochloride*,  $C_{26}H_{41}O_{11}N \cdot HCl$ ; measurements by Dr. Waller with sample obtained from Dr. Wyndham Dunstan (Trans., 1894, **65**, 290). Concentration = 1 per cent., or  $N/55$  (*Quart. J. Exp. Physiol.*, 1910, **3**, 102). The results are given in the table below.

TABLE VII.

I.	II.	II(bis).	III.	I.	II.	II(bis).	III.
0	19·8	—	—	12	13·5	13·8	0·0128
2	19·0	—	0·0056	14	13·0	13·0	0·0125
4	18·0	—	0·0088	16	12·3	12·3	0·0129
6	17·0	—	0·0099	18	11·5	11·7	0·0129
8	15·5	15·5	0·0124	20	11·0	11·0	0·0125
10	14·5	14·7	0·0123	22	10·3	10·5	0·0122

The above results show clearly an induction period, in that the chemical change commences slowly, increases to a maximum, and thence decreases proportionately to the remaining units of potential chemical change.

It would not be difficult to find in chemical literature a reaction of a lifeless chemical compound proceeding on an almost identical course.

The values in column II(bis) are calculated, after conclusion of the induction period, from a mean value,  $K=0·0125$ .

*Dimethylaminomethylidimethylcarbinol Benzoate Hydrochloride*,  $OBz \cdot CMg \cdot CH_2 \cdot NMMe_2 \cdot HCl$ , or the methyl analogue of the local anaesthetic, stovaine. Concentration,  $N/500$ . Temperature 17°.

The results are given below, the values in column II(bis) being calculated from a mean value of  $K=0·0150$ .

TABLE VIII.

I.	II.	II(bis).	III.	I.	II.	II(bis).	III.
0	15·0	—	—	8	7·0	6·7	0·0114
2	12·0	12·2	0·0485	10	5·0	5·2	0·0478
4	10·0	9·7	0·0442	12	4·0	4·2	0·0489
6	8·5	8·0	0·0411	14	3·0	3·5	0·0435

The values in this series are rather less concordant than those of other sets of experiments; possibly this may be due to irregularities

caused by a slight separation of the free base, which can be caused even by traces of alkali dissolved out from soft glass.

*Cinchonamine Hydrochloride, N/1000.*—The results obtained with this substance (kindly supplied by Mr. D. Howard), the only poisonous alkaloid of the cinchona group, were very similar to those given in the preceding table.

*Non-electrolytes.*—The chemical changes which occur between muscle proteins and substances, such as the halogen derivatives of the hydrocarbons, are somewhat difficult to interpret; further, in most cases, the muscle goes into contracture more or less rapidly, so the results cannot be made the subject of mathematical analysis.

One set of experiments obtained with a N/100-chloroform solution, freshly prepared and cooled to 10° (both being necessary conditions), is given below (compare Veley and Waller, *Proc. Roy. Soc.*, 1910, *B*, 82, 212); the values in column II(bis) are calculated from a mean value of  $K = 0.0298$ .

TABLE IX.

I.	III.	II(bis).	III.	I.	II.	II(bis).	III.
0	18.5	—	—	12	5.5	8.2	0.0282
2	16.9	16.2	0.9315	14	7.7	7.2	0.0289
4	14.0	14.0	0.9303	16	6.5	6.2	0.0279
6	12.0	12.0	0.9313	18	5.2	5.4	0.0266
8	10.5	10.7	0.9308	20	4.5	4.7	0.0244
10	9.5	9.5	0.9290				

Other sets of experiments obtained with chemical compounds of various types might be given, but it is thought that the selection given is sufficient to establish the general principle that the reactions between chemical compounds and living muscle-proteins follow the course of reactions of the first order, and are expressible by the general equation of this type of change.

#### *Rate of Chemical Change a Linear Function of Time.*

It must be admitted that such cases do not afford such conclusive evidence as to the chemical nature of the change as those in which the rate is a logarithmic function of time, but they do not necessarily militate against the hypothesis, as certain chemical reactions do proceed as a linear function of time.

It was shown by Jones and Richardson (*Trans.*, 1902, **81**, 1146) that such changes involve the simultaneous production from one substance of at least two others, whilst the rate of formation of each of the latter is directly proportional to the amounts of the original substances present. Since the work of these chemists, Cain and Nicoll (*Trans.*, 1903, **83**, 208) and the author (*Trans.*, 1903, **95**, 1186) have studied chemical changes of this type, represented by the simple equation  $K = \Delta r / \Delta t$ , in which  $r$  = the number of

potential units of chemical change,  $t$ =time, and  $K$ =factor of chemical change. Suitable examples of the kind investigated are given.

*Ethyl Alcohol, N/10, at 17°.*

The results are given below: in column I, the times from start ( $t$ ); in II, the number of units of potential change ( $r$ ) expressed in the same terms as before; and in column III the values of  $\Delta r/\Delta t$  or  $K$ , the factor of chemical change.

TABLE X.

I.	II.	III.	I.	II.	III.
0	19.5	—	8	7.5	1.7
2	17.0	1.3	10	4.5	1.5
4	14.0	1.5	12	1.5	1.5
6	11.0	1.5			

The figures in the third column lead to a mean value  $K=1.5 \pm 0.2$ .

*Trichloroethylene, N/150.*—Two cases have been given in a previous paper (*Proc. Roy. Soc.*, 1910, *B*, **82**, 224), giving the same mean value for  $K$ , namely, 1.5, so that it is unnecessary to reproduce the figures. The general conclusion arrived at was that an arc of a curve had become almost coincident with the chord, or, in other words, the rate of chemical change was on a boundary line between an exponential and linear function of time.

*The Effect of Fatigue.*—As the view has been held that the action of a drug is nothing else than an accelerated process of fatigue, a blank experiment was conducted at a temperature of 20°, in which the muscle was immersed throughout in the salt solution. In the following table, the times are given in column I, and the heights of response in millimetres in column II.

TABLE XI.

I.	II.	I.	II.
0	17	16	13
2	17	18	12
4	17	20	11
6	16	22	11
8	16	24	10
10	15	26	10
12	14	28	10
14	14	30	9

It will be evident, on inspection of the above figures, that in the first interval of 4' there was no effect, but from this point there was a slow decline approximately as a *linear* function of time, and even after 30' the height of the response, taken as a measure of the change, was reduced by less than 50 per cent.

It must, of course, be admitted that there is a slight fatigue

effect superadded to that of the chemical compound in the experiments described above, which would tend to increase the value of the constant  $K$  (the factor of chemical change), but its effect is not of a sufficient order to interfere with the logarithmic ratio of a reaction of the first order.

It was pointed out in the text above that if the change consisted in a chemical reaction between an acid or base or amino-acids or polypeptides, then it would follow as a logical consequence that an amino-acid would produce no effect, provided, of course, that the solution was not so hypertonic as to produce a complication resulting from an osmotic effect.

The results are given in the succeeding table with a  $N/25$ -solution of aminoacetic acid; the figures have the same significance as those in table XI.

TABLE XII.

L.	II.	I.	II.
0	18.0	14	13.5
2	17.0	16	12.5
4	17.0	18	12.0
6	16.0	20	11.5
8	15.0	22	11.0
10	14.5	24	10.0
12	14.0		

On a comparison of the last two tables, it is manifest that the values in both are identical within the limits of experimental error, or, in other words, the results given in table XII are merely those of fatigue effects, and the aminoacetic acid takes no part in the matter.

A  $N/10$  solution of aminoacetic acid, namely, twenty times the concentration of the acetic acid solution examined (table V), was found to be hypertonic, and produced an osmotic effect.

In the case of other amphoteric electrolytes, the author has elsewhere (*Quart. J. Exp. Physiol.*, 1910, **3**, 237) pointed out that as the affinity value of the acid function ( $K_a$ ) increases, the chemical effect likewise increases. The substances examined were tyrosine, cacodylic and aspartic acids, but other substances of the same type might also be tried.

#### Summary.

The main points of the present communication are as follows:

(1) When a living muscle is immersed in solutions of certain compounds, a *chemical change* takes place between the solute and the muscle proteins or their initial hydrolysis products; its rate can be measured by the heights of response to induction shocks used as an indicating record.

(2) In most cases the rate of change is a logarithmic function of

time represented by the equation of a reaction of the first order, namely,  $K = 1/t(\log r_0/r_t)$ , in which  $r_0$  is the number of units of potential chemical change when  $t=0$ , and  $r_t$  the number of units remaining after expiry of time  $t$ .

In a few cases, the rate of change is a linear function of time, which, although less conclusive, does not exclude the possibility of a chemical change.

(3) The effect of fatigue from induction shocks with the application of sodium chloride solution only produces a slowly diminishing result, and, as would be expected, no effect is at first apparent, and then the decrease of response is a linear function of time.

(4) If the hypothesis be correct that the chemical changes discussed under (2) are due to a reaction between the compounds, whether acid or base, and the polypeptides, either formed by hydrolysis of the muscle-protein or present by virtue of the moribund condition of the muscle, then amino-acids in not too highly concentrated solution should produce no effect. Results are given in the case of aminoacetic acid in proof of this line of argument.

In conclusion, it may be remarked that it is not to be expected that results obtained with a still living animal tissue would be of the order of accuracy of those between compounds purified with the refined art of the chemist; one comparison of these two lines of investigation show that the possible accuracy of the former is not greatly inferior to that of the latter type.

THE PHYSIOLOGICAL LABORATORY,  
THE UNIVERSITY OF LONDON.

XXIII.—*Studies of the Constitution of Soap in Solution: the Electrical Conductivity of Sodium Stearate Solutions.*

By RICHARD CHARLES BOWDEN.

THE study of the constitution of soap solutions is of the greatest importance in a large number of directions, both practical and theoretical. One of the most obvious problems still awaiting explanation arises out of the fact that there is no reason for suspecting the existence of any colloid whatsoever in solutions of sodium acetate, whilst it is equally impossible to deny the existence of

colloids in the solution of the salts of the higher homologues of this series. The question as to whether, say, sodium palmitate,  $C_{16}H_{32}O_2Na$ , itself is a colloid or an electrolyte is at present still entirely open, although it seems more probable that it is an electrolyte (McBain and Taylor, *Zeitsch. physikal. Chem.*, 1911, **76**, 1; *Ber.*, 1910, **43**, 321; compare Ubbelohde and Goldschmidt, *Handbuch der Chemie und Technologie der Oele und Fette*, Vol. 3).

Since the classical work of Chevreul, there are very few papers bearing directly on this problem. The boiling-point investigations of Kraft and his collaborators have become classical, but unfortunately the method has been shown to be quite untrustworthy (McBain and Taylor, *loc. cit.*) on account of the impossibility of removing dissolved and "sorbed" (McBain, *Phil Mag.*, 1909, [vi], **18**, 916; *Zeitsch. physikal. Chem.*, 1909, **68**, 471) air from the easily frothing, viscous solutions. Smits' vapour-tension work suffers from the same defect. The conductivity measurements of Kahlenberg and Schreiner (*Zeitsch. physikal. Chem.*, 1898, **27**, 552) in dilute solution unfortunately did not go far enough to give information about the concentrated solutions under discussion.

The investigations of McBain and Taylor have revealed some unexpectedly interesting results, in that, for example, they have shown that the equivalent conductivity of sodium palmitate passes through a pronounced maximum at a concentration of  $N/2$ , and a well-defined minimum at a concentration of  $N/5$ . Such a phenomenon has never before been met with in aqueous solution, although exactly similar cases occur in non-aqueous solutions (compare Franklin and Gibbs, *J. Amer. Chem. Soc.*, 1907, **29**, 1389).

The present paper contains measurements of the conductivity of solutions of sodium stearate,  $C_{18}H_{32}O_2Na$ , carried out in order to observe the effect of the addition of two  $CH_2$  groups on the form and position of the conductivity curve. The result has been that, although, like sodium palmitate, sodium stearate is an excellent conductor at all concentrations, yet the values of its conductivity differ markedly from those of the palmitates, and the maximum and minimum of the conductivity curve have been considerably displaced.

The experimental method has been fully described in the paper of McBain and Taylor. The method is that of Kohlrausch, using telephone and induction coil. The solutions were made up and shaken until homogeneous in pure silver tubes, and they did not come into contact with the Jena-glass of the dipping electrodes until a few minutes before the actual reading. The stearic acid was recrystallised twice from absolute alcohol, and melted at  $69\text{--}45^\circ$ .

The "resistance capacity" of the dipping electrode was, on

account of the conductivity of the outer silver tube, a function of the observed resistance. It was measured in solutions of specially purified potassium chloride of concentration  $N$ ,  $N/10$ ,  $N/50$ , and  $N/100$ , and also in a saturated solution of specially purified sodium chloride.

The values obtained were within one per cent. of those determined a year previously by Miss Taylor. All vessels and instruments were carefully calibrated.

The work of McBain and Taylor has shown that in the case of sodium palmitate, the conductivity of a given solution is the same within the limits of experimental measurement, whether the solution is prepared by dissolving pure sodium palmitate, or by mixing sodium hydroxide solution with an equivalent amount of palmitic acid. Hence it seemed safe to make the same assumption in the case of the stearate, and to prepare the solutions by mixing pure sodium hydroxide (from sodium and conductivity water) with stearic acid. The solutions were shaken in each case for about the same length of time as the corresponding palmitates. In the following table the first column gives the weight-normality, the second the number of grams of sodium stearate in 100 grams of water, the third the capacity factor of the electrode, the fourth the specific conductivity in mhos at  $90^{\circ}\text{00}^{\circ}$ , the fifth the density (due to E. C. V. Cornish, *Zeitsch. physikal. Chem.*, 1911, **76**, 32), the sixth the molar or equivalent conductivity at  $90^{\circ}\text{00}^{\circ}$ , and the last the final results for the equivalent conductivity.

*Sodium Stearate at  $90^{\circ}\text{00}^{\circ}$ .*

I.	II.	III.	IV.	V.	VI.	VII.
0.479	29.98	3.77	0.96326	(0.9547)	57.98	83.33
			0.96371		88.65	
			0.94194		77.52	
0.4942	15.14	3.75	0.93106	0.9600	75.57	76.1
		3.574	0.93115		75.66*	
0.1988	6.088	3.72	0.91393	0.9632	77.34	77.44
			0.91395		77.31	
0.0997	3.054	3.70	0.907105	0.9642	76.15	76.05
			0.907086		75.95	
0.0499	1.529	3.675	0.903680	0.9648	77.59	77.98
			0.903716		78.36	
0.00999	0.306	3.60	0.901298	0.9652	125.6	125.9
			0.901213		126.2	

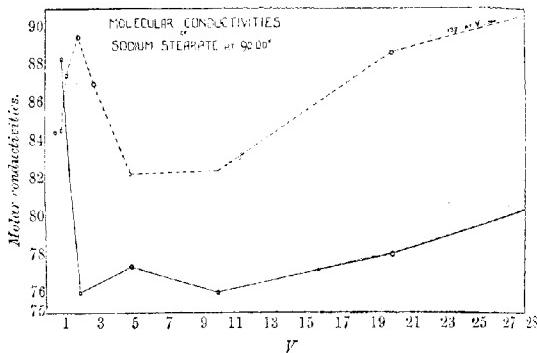
\* A perfectly independent measurement made at another time by Miss Taylor.

Both the molar and the specific conductivities contain a correction of 0.1 per cent. (subtracted) on account of the thermal expansion of the electrodes.

The results are sufficiently remarkable. The conductivity remains nearly constant at the value of 77 mhos between the concentrations

$N/2$  and  $N/20$ , the values then rising by 12 per cent. to 88.3 for the normal solution, and to 125.9 for the  $N/100$ -solution. The figure below shows their conductivity values plotted against the volume of water in litres containing 1 gram-molecule of sodium stearate, and the values for sodium palmitate are also plotted for comparison.

In the first place, these high values obtained for the conductivity even of the most concentrated solutions prove that much electrolyte is present, and that therefore soaps cannot be simple colloids (compare Kraft and his co-workers, *Ber.*, 1894, **27**, 1747, 1755; 1895, **28**, 2566, 2573; 1896, **29**, 1328; 1899, **32**, 1584; Smits, *Zeitsch. physikal. Chem.*, 1903, **45**, 608). On the other hand, the presence of a colloid in these solutions cannot well be denied; it



seems therefore that the colloids present are the acid sodium salts  $C_{16}H_{32}O_2C_{16}H_{31}O_2Na$  and  $C_{18}H_{36}O_2C_{18}H_{35}O_2Na$ . The peculiar shape of the conductivity curve might be explained as due to the change in the degree of dispersion of the colloid. Acid sodium salt (containing an excess of sodium depending on the concentration of the free alkali in the solution) is found in dilute alkaline solution, such as the dilute soap solutions, in the form of a coagulated precipitate; it is also precipitated quantitatively (salted out) by excess of free alkali.\* Intermediate solutions, such as the concentrated sodium stearate and sodium palmitate solutions, are opalescent or

\* McBain and Taylor, *loc. cit.*; thus the coagulated precipitate in equilibrium with a 1.6-N-solution of sodium hydroxide has the empirical composition of 54 per cent.  $C_{16}H_{31}O_2Na$  + 41 per cent.  $C_{16}H_{32}O_2C_{16}H_{31}O_2Na$ , as calculated from the decrease in concentration of the sodium hydroxide solution employed for the salting out.

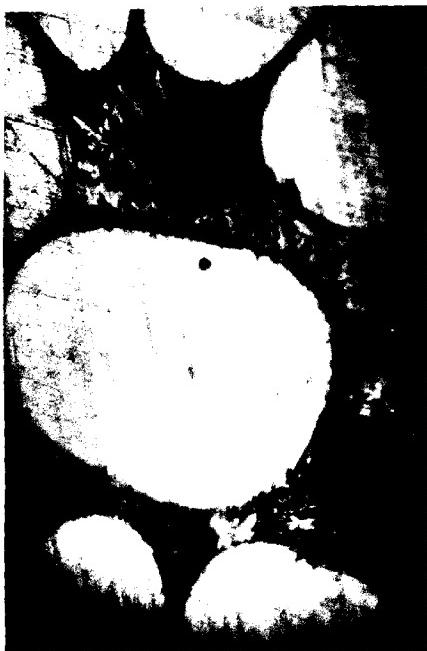


Microphotograph, No. 9.

25 per cent. silver; 75 per cent. tin, cooled "at a medium rate."

Magnification: 50 diameters; colored by HCl.

Two elements: dark gray color; others: and light  
crystalline  $\text{Ag}_3\text{Sn}$ .



Microphotograph, No. 57.

501 parts out silver; 501 parts out, thin, quenched after one hour  
at 400°.

Magnification: 300 diameters; etched by KCN.

The elements: dark granular: cubic and light  
crystalline:  $\text{Ag}_2\text{S}$ .

even quite transparent, depending on the concentration. Thus, the conductivity results might be explained by the sorptive powers of the colloidal acid salt decreasing so much as its degree of dispersion increased that the relative amount of free hydroxide in the solution increases for a time with increase of concentration. In still stronger solutions one might expect more and more of normal salt to be formed, and this, together with lessening dissociation, would explain a second decrease in the conductivity in the strongest solutions.

However, as this problem is being attacked from many different points of view in this laboratory, it would be premature as yet to regard this as being more than a plausible explanation which is in agreement with all the facts.

My sincere thanks are due to Dr. James W. McBain, at whose suggestion this work was undertaken, for his continued interest and advice.

CHEMICAL DEPARTMENT,  
UNIVERSITY, BRISTOL.

#### XXIV.—*Amalgams Containing Silver and Tin.*

By REGINALD ARTHUR JOYNER.

The object of the present investigation was to ascertain the chemistry and physical chemistry of the ternary system—tin, silver, and mercury. Our knowledge of this system is as yet due entirely to empirical experience in dental practice\* and to isolated measurements, chiefly of changes in form and of crushing strength.

Dentists have had no clue to the reasons for uncontrollable differences in behaviour of their amalgams, and hence the elucidation of the chemical changes involved appeared not only interesting from the purely scientific point of view, but fundamentally necessary for further progress in this most important branch of dental metallurgy.

Before studying the more complicated system containing the three constituents, it was obviously necessary to complete our

\* Dental amalgams consist essentially of alloys of tin and silver in various proportions, amalgamated with somewhat less than their own weight of mercury. Usually several per cent. of various other metals are added in the endeavour to obtain a so-called "benevolent" effect on the amalgam, which generally takes its name from one of these slight admixtures, for example, "gold" or "platinum" amalgam.

knowledge of the three pairs of metals taken separately. Two of these systems, mercury-tin and mercury-silver, have been thoroughly and satisfactorily studied by other investigators (see p. 204). On the other hand, certain remarkable properties of the silver-tin alloys which have been discovered by dentists have never been mentioned or accounted for in chemical literature. Thus a thorough revision of previous work on these alloys was necessitated.

#### EXPERIMENTAL.

Great care was taken in the preparation of the metals studied, as the use of impure constituents might explain the discrepancies between the results of previous investigators. Silver chloride, prepared by dissolving silver in nitric acid and precipitating, was dissolved in ammonia, the solution filtered, and precipitated as chloride. This was fused with sodium carbonate, and the silver treated in a molten state successively with potassium nitrate, ammonium chloride, and borax, a bone ash support being employed. Best commercial tin was dissolved in hydrochloric acid; the stannous chloride which crystallized out was converted into metastannic acid by nitric acid; this was dried, and then reduced by coal gas or hydrogen in a combustion furnace. The finely divided tin thus obtained was fused under potassium cyanide and cast into bars.

Dentists have long held that the alloys of silver with tin, which constitute the essential portion of dental amalgam alloys, undergo profound changes in their properties merely through lapse of time. This phenomenon is technically called "ageing," and it is taken into account in dental practice, although not much is definitely known in regard to it.

In 1895-1897, G. V. Black published a series of researches bearing on this subject (*Dental Cosmos*, 35-39), and his results have since been given unquestioned authority. He found that fresh filings of these alloys required half as much mercury again for amalgamation as was required by similar filings which had been kept for some months, or which had been heated for half an hour to 100°. Exclusion of air did not affect these results. Again, the amalgams made from freshly prepared filings showed quite different volume changes from those exhibited by the amalgams made from "aged" filings.

Petrenko (*Zeitsch. anorg. Chem.*, 1907, 53, 200) has studied the silver-tin alloys in Tammann's laboratory, applying the modern methods of thermal analysis and of micro-photography, and his is the most important and most recent work on the alloys in question. Evidently he was unaware of the dental literature bearing on the subject, for he confined his attention chiefly to the alloys containing

a very high percentage of silver (more than 75), whilst the dental alloys contain between 40 and 70 per cent. of silver. Further, as he himself emphasised, there is an important theoretical discrepancy in his results in that the transition of  $\beta\text{-Ag}_3\text{Sn}$ , stable above  $232^\circ$ , into  $\alpha\text{-Ag}_3\text{Sn}$ , stable below  $232^\circ$ , could not be detected when the alloy contained less than 50 per cent. of silver, although all the alloys lying between 35 and 75 per cent. of silver should consist, according to his results, of a mechanical mixture of pure tin with  $\text{Ag}_3\text{Sn}$ . In other words, the marked transition point of the  $\text{Ag}_3\text{Sn}$  at  $232^\circ$  had disappeared, whilst the alloy was still supposed to consist of  $\text{Ag}_3\text{Sn}$  to the extent of two-thirds of its weight. Thus, it seemed altogether probable that Petrenko had overlooked some compound between silver and tin lying in the region of the dental alloys. A satisfactory hypothesis could be found to explain all the facts if it were assumed that a compound such as  $\text{Ag}_3\text{Sn}$  existed and was rather slowly formed.

In the first place, the attempt was made to discover whether any alloy mixed in the proportions corresponding with  $\text{Ag}_3\text{Sn}$ ,  $\text{AgSn}$ ,  $\text{Ag}_3\text{Sn}_2$ , or  $\text{AgSn}_2$  would become homogeneous and solid when kept at constant temperatures lying between  $220^\circ$  and  $300^\circ$  for several days. In no case did the alloy completely solidify above the eutectic temperature,  $220^\circ$ .

These experiments alone cast much doubt on the possibility of the existence of any such new compound, for the latter must have existed above  $232^\circ$  in order to interfere with the transition of the  $\text{Ag}_3\text{Sn}$  at this temperature.

All the alloys of tin and silver (less than 75 per cent. of silver) have been systematically investigated with regard to their micro-structure. The alloys were submitted to various treatment (quenching in water from the molten condition; annealing for days in a molten lead bath; ordinary cooling in air, etc.), and then sections were etched by various reagents and examined in a Zeiss apparatus for metallography.

Two typical microphotographs are illustrated, facing pp. 194 and 195. The result was decisive; all the alloys containing less silver than corresponds with  $\text{Ag}_3\text{Sn}$  are unmistakably heterogeneous, no matter how prepared, or how annealed or given time to age.\*

\* It was noticed that almost always the alloys contained at least traces of eutectic mixture. Ignorance of this point has been fatal to the work of previous investigators; thus, Herschikowitsch (*Zeitsch. physikal. Chem.*, 1898, **27**, 125) obtained only two sets of alloys; one of these, with a low percentage of tin, had nearly the same potential as pure silver, whilst all alloys containing more than 32 per cent. by weight of tin behaved like pure tin. These results were evidently due to the actual presence of pure tin in the second set and to approximately the same isomorphous mixtures of silver and  $\text{Ag}_3\text{Sn}$  in all the alloys of the first set.

Thus the results are conclusively in support of Petrenko's view that all alloys, if well annealed, contain only the compound  $\text{Ag}_3\text{Sn}$  and free tin, no other compounds being formed in any circumstances. If, however, the alloy contains more than 50 per cent. of silver, the first solid separating out consists of a solid solution of Ag in  $\text{Ag}_3\text{Sn}$  (compare Petrenko, *loc. cit.*), the pure  $\text{Ag}_3\text{Sn}$  only becoming stable below  $480^\circ$ ; when the cooling is not very slow, these solid solutions are partly retained in the solid castings.

#### *The Ageing of Filings of Alloys of Silver and Tin.*

Since the after changes in the properties of the solid filings, "ageing," may take place in the cold on merely keeping the filings for some time, the phenomena might be ascribed to some metastable condition of the alloys themselves. The section above, however, has shown that only one kind of metastability can occur in the tin-silver alloys, and this only in those alloys (containing more than 50 per cent. of silver) which are not completely fused at  $480^\circ$ . The dental literature and Black's date in particular describe as pronounced an effect due to "ageing" in the alloys low in silver as in those containing much of that metal.

In order to confirm the existence of, and to determine the extent of, "ageing," the following method was adopted. A weighed quantity of filings, about 1 grams, was shaken with excess of mercury for exactly two minutes, and thereupon the excess of mercury was squeezed out through a small bag of chamois leather by a 56lb. weight applied through a piston in a cylinder 20 cm. in diameter. The weight was applied four times in succession, each time for thirty seconds, and it was gently rocked so that the loosely fitting piston just moved in the cylinder.

No amount of squeezing will remove all excess of mercury, but it was found that the amounts squeezed out in duplicate experiments were sufficiently constant.

In the present paper, the proportions of the silver-tin alloys are expressed in atomic percentages throughout.

If a certain amount of filings, taken immediately after filing, be treated with excess of mercury as above, a definite value is obtained for the ratio of the weight of mercury retained in the residue to the original weight of filings taken.\* Thus, for example, the first two values in table I were obtained from an alloy of 60 atomic per cent. of tin and 40 atomic per cent. of silver, the ratio of mercury to alloy found being 0·78 and 0·88. Such filings, freshly prepared by filing up a cast ingot of alloy, are termed "unaged" when the

\* Owing to the very low solubility of tin and silver at room temperature, the mercury squeezed out removes only a negligible amount.

filings have not been subjected to further treatment before amalgamation.

TABLE I.

Composition of alloy.	Weight taken.	Mercury retained.		Ratio mercury/alloy.
		Unaged.	Aged.	
Silver: 40 per cent. ....	4.37	3.42	—	0.78
" " "	4.67	4.14	—	0.88
" " "	4.47	—	1.84	0.41
" " "	4.68	—	1.89	0.41

The last two results in table I were obtained from the same filings, but these were heated for thirty minutes in an atmosphere of hydrogen at 100° before amalgamation. It is seen from the table that these "aged" filings retained only half the amount of mercury that the "unaged" filings did, namely, 0.41, instead of 0.83 of their weight.

The existence of this unique phenomenon is thus demonstrated.

It must be clearly borne in mind in the following discussion that no method of measurement or even of detection of this property is known other than that already described. When a cast bar of alloy is freshly filed, with the utmost care to avoid unnecessary force or opportunities of heating, the filings are by definition "unaged." When these filings are heated for some time at 100° they become "aged," as is seen by the relatively much smaller amount of mercury retained immediately after amalgamation.

However, after these experiments have once been carried out carefully with filings from a cast bar, more or less definite numbers are obtained for each percentage composition of the alloy which represent the two weights of retained mercury corresponding with the states "aged" and "unaged" respectively. Hence, when an amalgamation test of any alloy of a given percentage composition is compared with the two standard values representing the "aged" and "unaged" states, an extension of the above definition permits of the use of the terms, "unaged," "aged," "partly aged," in describing the alloy in question, even although the filings tested are freshly prepared from a solid bar. It will be noted that the terms apply directly only to filings, and not to the massive metal.

It will be of advantage to summarise the following results for reference in advance before discussing the experimental details.

A. The following preparations behave similarly to standard "unaged" filings: (1) Carefully filed fresh filings of all bars of cast alloy; (2) carefully filed fresh filings of all bars of "recemented" alloys containing more than 35 per cent. of silver, no matter at what temperature the "recementation" of the filings took place.

B. The following preparations were "aged": (1) All filings of alloy (not pure tin) which had been heated for an hour at 100°, with or without the exclusion of air; (2) all recemented filings from bars containing less than 25 per cent. of silver, no matter at what temperature the recementation took place; (3) many filings which were obtained by vigorous filing.

It will be readily understood that most of the filings examined were neither completely "aged" nor ideally "unaged." The unsatisfactory nature of the only method of examination available also prevented the results from possessing any high degree of accuracy; the accuracy attainable, under good conditions, hardly exceeded one unit of the first place of decimals in the ratio: mercury retained/weight of alloy.

In table II are given the standard numbers representing the "aged" and "unaged" states respectively for the various alloys. The composition of the alloy is expressed in atomic percentages of silver and tin, and also in percentage by weight of the compound Ag<sub>x</sub>Sn. The last two columns represent the difference in weight of mercury retained by one gram of "unaged" and "aged" filings, and the ratio between these two amounts of retained mercury.

TABLE II.

*Mercury Retained by "Aged" and "Unaged" Filings.*

Percentage composition of alloy.	"Unaged" filings.		"Aged" filings.		Diff. in Hg, "unaged," "aged,"	Ratio of Hg "unaged," "aged."
	Ag	Ag <sub>x</sub> Sn	Hg in alloy, amalgam.	% Hg in alloy, amalgam.		
75.0	100.0	2.12	68	0.68	41	1.33
—	—	2.08	67	0.78	44	—
—	—	—	—	0.66	40	—
70.0	82.8	1.79	63	0.86	46	0.81
—	—	1.60	61	0.82	45	—
55.0	72.0	0.92	43	0.37	27	0.53
—	—	0.86	46	0.35	26	—
40.0	51.7	0.98	49	0.33	25	0.52
—	—	0.83	44	0.41	29	—
—	—	0.78	44	0.41	29	—
—	—	0.88	47	—	—	—
—	—	0.89	47	—	—	—
—	—	0.92	48	—	—	—
35.4	45.4	0.89	47	0.49	33	0.40
25.0	31.7	0.86	46	0.52	34	0.34
10.0	12.6	0.77	41	0.19	33	0.28
3.84	4.77	0.56	35	0.64	40	—
—	—	0.59	37	0.57	36	—
—	—	0.45	31	0.43	30	—

\* Cooled in an electric furnace from 430—200° during a period of three days. The alloy was very slowly filed, and it was cooled under the water tap every ten seconds during filing. These values are relatively as well as absolutely the greatest which could be obtained.

Each of the following experiments was carried out in order to test a definite hypothesis in regard to the nature of "ageing," and they will therefore be dealt with in this order.

(a) Does a bar which has been heated to 100° for some time before filing yield "aged" filings?

Part of a cast bar containing 40 per cent. of silver was simply filed, whilst another part was annealed for half an hour in boiling water before filing.

Filings from cast bar gave ratio ..... = 0·89  
 ,,, annealed bar gave ratio ... = 0·92

Therefore it is necessary for the alloy to be in a state of fine division in order to become "aged," but the experiment says nothing as to whether or not "ageing" is due to mechanical shock of filing (compare Cohen's "forced metals," *Zeitsch. physikal. Chem.*, 1910, **71**, 301).

(b) Do filings of tin age? The experiment gave:

Ratio for fresh filings ..... = 0·48  
 ,,, annealed filings ..... = 0·45

Thus pure tin does not age at all.

Hence in contradiction of Black's own theory, the phenomenon of "ageing" is not connected with any change from one to the other of the four known modifications of pure tin (grey, white, orthorhombic, "forced").

(c) Is "ageing" connected with a possible suspension of the transition of  $\beta\text{-Ag}_3\text{Sn}$  (stable above 232°) to  $\alpha\text{-Ag}_3\text{Sn}$  (stable below 232°)?

Possibly, as Rosenthal and Tucker (*Phil. Trans.*, 1908, A, **209**, 89) have suggested in the case of lead-tin alloys, the tin forms a protective sheath round the metastable  $\beta\text{-Ag}_3\text{Sn}$  crystals.

Here, then, the act of filing might regularly convert the stable  $\alpha\text{-Ag}_3\text{Sn}$  into metastable  $\beta\text{-Ag}_3\text{Sn}$ , and annealing at 100° would then restore the filings to the stable form; thus the difference between "unaged" and "aged" filings would be merely the difference in reactivity (or possibly the path of the reaction) with mercury of the metastable  $\beta\text{-Ag}_3\text{Sn}$  and the stable  $\alpha\text{-Ag}_3\text{Sn}$ .

Now the alloys under consideration consist of the compound  $\text{Ag}_3\text{Sn}$ , which does not melt below 480°, with eutectic mixture, which melts at 220°, that is, 12° below the transition point. Therefore these alloys can be partly melted without any chance of the transformation taking place on re-cooling; such bars differ neither in appearance nor hardness from the original alloys. This procedure has been termed "recementation" of the filings. When a recementation experiment took place above 232° and a small piece of  $\beta\text{-Ag}_3\text{Sn}$  was dropped into the semi-fluid mass, every chance was

given for the conversion of the  $\alpha$ -Ag<sub>3</sub>Sn into the  $\beta$ -Ag<sub>3</sub>Sn, particularly as in these cases the alloy was afterwards cooled quickly.

The following results were obtained, an atmosphere of hydrogen being employed in each case:

10 per cent. of Silver and 90 per cent. of Tin = 12·6 per cent. of Ag<sub>3</sub>Sn and 87·4 per cent. of Tin.

	Ratio Hg/alloy.
"Unaged" .....	0·77
"Aged" .....	0·49
Recemented below 230° (fresh filed) .....	0·58
" " 230° and then "aged" .....	0·55
" " above 230° (fresh filed) .....	0·54
	0·45

The alloy recemented below 230° yielded filings which were already "aged," and practically no metastable Ag<sub>3</sub>Sn could have been present. On the other hand, the recementation above 250°, which is the most favourable for retaining metastable  $\beta$ -Ag<sub>3</sub>Sn, did not produce "unaged" filings. The latter experiment is in direct contradiction of the hypothesis (c).

25 per cent. of Silver and 75 per cent. of Tin = 31·8 per cent. of Ag<sub>3</sub>Sn and 68·8 per cent. of Tin.

	Ratio.
"Unaged" .....	0·84
"Aged" .....	0·52
Recemented at 240–260° for one hour and fresh filed .....	0·52
	0·60
	0·48

These results are likewise opposed to hypothesis (c).

35·4 per cent. of Silver and 64·6 per cent. of Tin = 45·4 per cent. of Ag<sub>3</sub>Sn and 54·6 per cent. of Tin.

	Ratio.
"Unaged" .....	0·89
"Aged" .....	0·49
Recemented below 228° (fresh filed) .....	0·72
" " 227° " .....	0·55
" " 225° " .....	0·78
	0·79

This alloy yields "unaged" filings even when no chance has been given (except during the act of filing, and for this compare the preceding alloys) for the stable  $\alpha$ -Ag<sub>3</sub>Sn to turn into metastable  $\beta$ -Ag<sub>3</sub>Sn. This also does not accord with hypothesis (c).

10 per cent. of Silver and 60 per cent. of Tin, or 51·7 per cent. of Ag<sub>3</sub>Sn and 48·3 per cent. of Tin.

	Ratio.
" Unaged " .....	0·98
" Aged " .....	0·83
Reheated below 283° freshly filed .....	0·35
" 228° " .....	0·74
" " .....	0·64

This alloy is similar to the last one.

The above results are remarkable in themselves, and do not seem to permit of explanation as yet.

(d) Is "ageing" the release by annealing of a state of strain induced by the act of filing?

The experiments with the 10 per cent. of silver and the 25 per cent. of silver alloys just cited are sufficient to disprove this, for their filings failed to produce "unaged" filings from a normally hard bar of metal.

(e) Is "ageing" a property of the Ag<sub>3</sub>Sn contained in the alloys?

If the difference between the ratios in table II is plotted against the amount of Ag<sub>3</sub>Sn in the alloys, a continuous curve is obtained, and when the inaccuracy of the data is borne in mind, it seems to indicate a direct proportionality between the capacity of an alloy for "ageing" and its content of Ag<sub>3</sub>Sn. Hence the property of "ageing" seems to belong to the Ag<sub>3</sub>Sn contained in all these alloys.

(f) Is "ageing" due to the oxidation of the Ag<sub>3</sub>Sn particles?

When filings are heated to 100°, whether in an atmosphere of hydrogen or in air, there is a slight colour change, which becomes more marked as the content of the Ag<sub>3</sub>Sn increases. This might be due to superficial oxidation of the tin in the compound. If, however, the surface tin were thus oxidised, silver would be left as a protective coating round each particle of "aged" Ag<sub>3</sub>Sn. Now mercury can penetrate through half an inch of tin in a few seconds (compare Roberts-Austen, *Introduction to the Study of Metallurgy*), but it amalgamates silver only partly even after many weeks (Fenchel, *Dental Cosmos*, 1910, 52, 24). Therefore, according to the hypothesis, each particle of Ag<sub>3</sub>Sn would be protected to some extent from the action of mercury by the silver round it.

Some 45 per cent. of silver alloy was prepared and filed, a part of the filings was "aged" and then ground in an agate mortar, whilst the other part was simply ground without "aging":

$$\begin{array}{ll} \text{Ratio for "unaged" pulverised} & = 1\cdot06 \\ \text{,, "aged" ,,} & = 0\cdot42 \end{array}$$

Thus the pulverisation had not "unaged" the latter alloy, even though the pulverised filings must have offered entirely unpro-

tected fresh surfaces for the action of mercury. This renders hypothesis (*f*) untenable.

To sum up, "ageing" is a property of the  $\text{Ag}_3\text{Sn}$  contained in the alloys, and a state of fine division is essential for its occurrence; pulverising "aged" filings does not "unago" them. Probably electromotive force measurements would throw light on the phenomena. It seems as if the only possible explanation left is that "ageing" is due to polymerisation of the  $\text{Ag}_3\text{Sn}$  (compare the relationships found by Allmand in the case of copper hydroxide, Trans., 1909, **95**, 251; 1910, **97**, 603).

It will be seen below that "ageing" does not affect the nature of the amalgam finally obtained, provided that excess of mercury is present.

It was found that no more mercury is taken up either by "aged" or "unaged" filings after a few days, and the final proportion of mercury retained in the solid is the same in both cases; this, in confirmation of the results of the solubility measurements to be described, shows that the solid amalgams ultimately obtained from "aged" filings are identical with those made from "unaged" filings.

Thus the sole effect of "ageing" is to retard the initial stages of amalgamation.

#### *Tin Amalgam.*

Tin amalgam has been most thoroughly studied by W. J. van Heteren (*Zeitsch. anorg. Chem.*, 1904, **42**, 129). He determined the melting points of all amalgams from pure tin to 5 atomic per cent. of tin, which melted at  $65^\circ$ .

The following table contains all his analyses of the liquid phase together with some further determinations:

Temperature.	Tin in liquid phase.		
	van Heteren.	Joyner.	
18.8°	0.36 atomic per cent.	—	—
0.0	0.59     "     "	—	—
14.0	—	—	—
15.0	0.97     "     "	—	—
25.0	1.21     "     "	—	—
25.1	—	1.24     "     "	—
63.2	—	4.04     "     "	—
90.0	—	18.0     "     "	—
163.0	—	66.7     "     "	—

From electromotive force experiments, he concluded that no compound between tin and mercury exists, but solid tin amalgam is simply mixed crystals containing about 1 per cent. of mercury.

*Silver Amalgam.*

The constitution of the silver amalgams at the ordinary temperature has been finally established by the thorough investigation of Ogg (*Zeitsch. physikal. Chem.*, 1898, **27**, 285) and Reinders (*ibid.*, 1904, **54**, 609). Only the compounds  $\text{Ag}_3\text{Hg}$ ,  $\text{Ag}_3\text{Hg}_2$ , and  $\text{Ag}_3\text{Hg}$  can exist, and of these  $\text{Ag}_3\text{Hg}$ , commonly called "Arbor Juncæ," is the only one readily formed.

The following determinations of the composition of the liquid phase in equilibrium with the compound  $\text{Ag}_3\text{Hg}_4$  have been made:

Temperature.	Atomic per cent. of silver in liquid phase.
14°	0·07
25	0·082
30	0·086
63	0·19
90	0·34
163	1·13

Reinders obtained 0·076 atomic per cent. at room temperature.

*The Ternary System: Tin, Silver, Mercury.*

Chemical literature contains no data at all in regard to the alloys of mercury with silver and tin. The solid amalgam used for dental fillings are usually made by filling up the silver-tin alloy, rubbing it with mercury in the hand or in a mortar, and squeezing out some of the excess of mercury. The pasty, semi-crystallised solid so obtained hardens within the course of a few hours or days, although very slight changes of form and possibly of volume continue to take place for many months or years. This hardening is obviously due to chemical change, although it has been hitherto unexplained. The experiments which follow demonstrate conclusively that the chemical reaction results in the breaking up of the compound between the tin and the silver ( $\text{Ag}_3\text{Sn}$ ) in order to form the compound  $\text{Ag}_3\text{Hg}_4$ , leaving all the tin in the free state. As will be seen, other relationships hold at higher temperatures.

A comprehensive series of cooling curves of the various amalgams were taken, but the chemical changes involved are too slow for this method to be advantageous. It was found that all amalgams of tin and silver, even those that have long hardened, undergo partial fusion at 65–100°, and gradually become more completely fluid as the temperature is raised. No break in the cooling curves is met with at higher temperatures. This means that there are only two groups of equilibria corresponding with higher and lower temperatures respectively.

*Investigation by Analysis of the Liquid Phase.*

The phase rule predicts that the solubility of a given component in the liquid phase must remain constant so long as any of this component exists free as a pure solid phase. A sudden break in the concentration in the liquid phase will thus occur when one of the two solid phases allowed by the phase rule disappears and is replaced by another. Should no compound exist containing both silver and tin in combination with mercury, the composition of the liquid amalgam is constant independent of the relative proportions of the metal in the solid phase. This simplest case is realised in the present system at room temperatures.

The following procedure was finally adopted. An alloy of definite proportions was prepared, filled, and placed in a glass tube, and on the tube being filled with hydrogen, mercury in excess was added, and the tube sealed off. The tube was then placed in a thermostat, and was frequently shaken. It was found that equilibrium is attained in about a week, but a fortnight was allowed. For analysis the tube was opened, and by means of a glass tube with a plug of glass-wool in the end, a quantity of the liquid phase, free from solid, was withdrawn by means of a pipette. This was weighed dissolved in 100 c.c. of nitric acid (1:4), and the solution boiled for a minute or two, this being necessary to convert the mercurous nitrate into the mercuric salt. After the evolution of brown fumes had ceased, water was added (200 c.c.), and the solution again brought to the boiling point and then allowed to settle. The metastannic acid thus formed was collected and estimated in the usual way. To the filtrate, the calculated amount of ammonium chloride necessary to convert all the mercuric nitrate to mercuric chloride was added. The above precautions are necessary, since silver chloride is soluble in solutions of mercuric nitrate (*Trans.*, 1908, **93**, 1405), and is therefore not completely precipitated as long as any of the latter salt remains. To free the silver chloride, which was formed in a very finely divided condition, from small amounts of calomel, the precipitate was treated with ammonia solution, the silver being reprecipitated by nitric acid. The silver chloride was then estimated in the usual way.

In all the experiments described, the amount of solid alloy added to the mercury was at least double the amount necessary to saturate the mercury with tin.

The following experiments were carried out with "aged" filings at  $25\cdot40^\circ \pm 0\cdot01^\circ$ .

TABLE III.

Alloy.	Percentage of tin in liquid amalgam.	Percentage of silver in liquid amalgam.
100 per cent. of tin	0·743	—
60 " "	0·751	—
80 " "	0·750	—
70 " "	0·760	0·045
60 " "	0·743	0·046
50 " "	0·748	0·048
40 " "	0·762	0·050
30 " "	0·751	0·049
20 " "	0·743	—
10 " "	0·752	—
0 " "	—	0·043
Average .....	0·751	0·045

A repetition of the above experiments, using double the amount of "aged" filings for the same amount of mercury, gave the following results (there was not enough liquid phase for analysis in the experiments, using 10 and 20 per cent. of tin):

TABLE IV.

Alloy.	Percentage of tin in liquid amalgam.	Percentage of silver in liquid amalgam.
50 per cent. of tin	0·751	0·043
40 " "	0·755	0·040
65 " "	0·748	0·046
70 " "	0·756	0·044
Average .....	0·753	0·043

Finally, the following experiments with "unaged" filings were carried out, but at  $25\cdot6^\circ \pm 0\cdot01^\circ$ :

TABLE V.

Alloy.	Percentage of tin in liquid amalgam.	Percentage of silver in liquid amalgam.
20 per cent. of tin	0·750	0·033
60 " "	0·760	0·044
78 " "	0·764	—
Average .....	0·758	0·041

These striking tables demonstrate conclusively that at room temperature no solid amalgam exists containing both silver and tin. The silver amalgam, which has the composition  $\text{Ag}_3\text{Hg}_2$  (Reinders and Ogg, *loc. cit.*), exists quite independently of the solid tin amalgam, which is a solid solution of a per cent. or so of mercury in tin. Again, the solid amalgams, formed from the "aged" filings, are identical with those obtained from "unaged" filings, since the analyses of the saturated liquid

amalgams do not differ by more than 0·8 per cent. of the 0·75 per cent. of tin present.

Similar experiments were carried out at  $63\cdot05^\circ \pm 0\cdot15^\circ$  with the following results:

TABLE VI.

Alloy	Percentage of tin in liquid amalgam.	Percentage of silver in liquid amalgam.
0 per cent. of silver	2·85	—
0 " "	2·36	—
*0 " "	2·36	—
0 " "	2·34	—
*20 " "	2·58	0·184
*30 " "	2·52	0·177
*50 " "	2·56	0·185
60 " "	2·60	0·184
80 " "	2·56	0·175
100 " "	—	0·100
" " "	—	0·103

Cohen and Inouye (*Zeitsch. physikal. Chem.*, 1910, **71**, 626), in a recent paper on zinc amalgam, have emphasised the magnitude of the inaccuracy possible in such solubility determinations at higher temperatures. Hence in the measurements marked with an asterisk a filter of chamois leather attached to a suction pump was employed for drawing off the liquid amalgam for analysis. It is satisfactory to note that this made no difference in the results.

It is evident that at  $63^\circ$  the only two solid phases occurring are still the compound  $\text{Ag}_3\text{Hg}_4$  and the solid solution of mercury in tin. The solubility curve of solutions saturated with respect to both mercury and tin forms a very flat curve through the three known points, and thus measurements at intermediate temperatures have been unnecessary.

Thus the general form of the ternary diagram is established for the temperatures from the melting point of mercury up to  $63^\circ$ .

There is no eutectic mixture, since the solubility of tin and of silver both become immeasurably small well above the solidification point of mercury.

The simple relationships which have been found for temperatures up to  $63^\circ$  do not hold at higher temperatures. There is a sharp transition point near  $70^\circ$  with the formation of a ternary compound, possibly  $(\text{Ag}_3\text{Sn})_2\text{Hg}$ ; this will form the subject of a further communication.

In conclusion, I wish to express my sincere thanks to Dr. James W. McBain for the very kind help he has given me in my work, which was undertaken at his suggestion.

CHEMICAL DEPARTMENT,  
UNIVERSITY, BRISTOL.

*XV.—Additive Compounds of Phenols and Phenolic  
Ethers with Aromatic Polynitro-derivatives.*

By JOHN JOSEPH SUDBROUGH and STANLEY HOSKINS BEARD.

ATTENTION has already been drawn to the readiness with which arylamines combine with aromatic polynitro-compounds (*Trans.*, 901, **79**, 522; 1903, **83**, 1334; 1906, **89**, 583; 1910, **97**, 773), and it has been shown that the effects produced on the colour of the additive compound by the introduction of substituents into the arylamine molecule are exactly parallel to the effects produced by the same substituents on the auxochromic nature of the primary amino-group. It is well known that the hydroxyl group is an auxochrome, although not so powerful as the amino-group. We were therefore induced to determine whether phenols and their derivatives are also capable of forming coloured additive compounds with trinitrobenzene and similar polynitro-derivatives.

The results show that such coloured additive compounds can exist, but that as a rule the colours of the compounds are not so pronounced as in the case of the additive compounds with arylamines. This is well shown by a comparison of the additive compounds which trinitrobenzene forms with the naphthylamines and aphthols:

α-Naphthylamine and trinitrobenzene.....	Brick-red.
β-Naphthylamine      "      " .....	Deep brick-red.
α-Naphthol            "      " .....	Orange-yellow.
β-Naphthol            "      " .....	Canary-yellow.

Compounds of phenols with trinitrobenzene do not appear to have been prepared previously, but numerous examples of additive compounds of picric acid with phenols and phenolic ethers have been described, and recently Meldola (*Proc.*, 1908, **24**, 210) has prepared a stable red additive compound of β-naphthol with trimellitacetyl-mimophenol.

In our experiments with amines we were able to show that combination with trinitrobenzene takes place when the nitrogen atom of the imino-group forms part of a closed ring, for example, tri-phenylpyridine, tetrahydroquinoline, etc. We also find that when the oxygen atom forms part of a ring the compound is capable of combining with trinitrobenzene. The best example to illustrate this point is comarone,  $C_6H_4\begin{matrix} < \\ \text{CH} \end{matrix}\text{O}\begin{matrix} > \\ \text{CH} \end{matrix}C_6H_4$ , which yields a very pale yellow, crystalline, additive compound. Diphenylene oxide,  $C_6H_4\begin{matrix} < \\ \text{O} \end{matrix}C_6H_4$ , also forms a definite additive compound.

Ketones, for example, benzophenone, acetophenone, benzoin, benzil, and deoxybenzoin do not appear to form additive compound and when both CO and O groups are present in a ring system for example, xanthone,  $C_6H_4<CO>C_6H_4$ , and dimethylpyrone  $CO<CH:CM\epsilon>O$ , additive compounds with trinitrobenzene are not formed; in the case of coumarin, the formation of an additive compound is shown by an examination of the melting-point curve.

The various phenolic ethers also tend to form coloured additive compounds with trinitrobenzene; the colours of these compounds are, as a rule, yellow, but quinol dimethyl ether forms an orange-red additive compound, and asarone a deep prune-coloured compound. As regards colour, there is no marked difference between the compounds derived from the phenols and those derived from the ethers. Similarly, Hofmann points out that the auxochromic effect of the hydroxyl and methoxyl groups are very similar.

In a former communication (*loc. cit.*, p. 776) we have drawn attention to the fact that quinoline and substituted quinolines form nearly colourless additive compounds with trinitrobenzene. Our present results show that by the introduction of a hydroxyl group into the quinoline molecule, more stable and more deeply coloured additive compounds are formed with trinitrobenzene. The colour of the additive compounds is, as a rule, canary-yellow when the hydroxyl group is attached to the pyridine nucleus, but of a brown or brownish-green colour when the hydroxyl group is attached to the benzene nucleus.

A comparison of the behaviour of the isomeric pairs of compounds:

Eugenyl methyl ether.	<i>iso</i> Eugenyl methyl ether.
Safrole.	<i>iso</i> Safrole.
Apiole.	<i>iso</i> Apiole.

towards trinitrobenzene was of interest, as Bruni and Tornani (*R. Accad. Lincei*, 1904, [v], **13**, ii, 181) state that the compounds containing a propenyl group ( $\cdot CH:CH:Me$ ) form additive compounds with picric acid, whereas the isomerides containing an allyl group ( $\cdot CH_2:CH:CH_2$ ) do not form such compounds.

Our experiments prove that apiole and safrole and also *iso*apiole and *iso*safrole form additive compounds with trinitrobenzene. These compounds are comparatively stable, and can be crystallised from solvents. It is noticeable, however, that the colour of the compounds containing a propylene group are more pronounced than those containing an allylene group; thus, *iso*eugenol, *iso*eugenyl methyl ether, *iso*safrole, and *iso*apiole all yield brilliant red additive compounds, and asarone yields a prune coloured compound with

trinitrobenzene. The colours of the additive compounds are undoubtedly influenced by unsaturated linkings or subsidiary latent valencies in groups adjacent to the benzene nucleus. Thus, amines with the tervalent nitrogen atom (two latent valencies) directly attached to the benzene nucleus form deeply coloured additive compounds, phenols and phenolic ethers with the bivalent oxygen atom (two latent valencies) attached to the nucleus form less deeply coloured products, and compounds which possess phenolic oxygen and a propenyl side-chain both attached to the nucleus give deep red coloured compounds.

The fact that cyclic compounds containing both a carbonyl group and a bivalent oxygen atom in the ring do not readily form additive compounds with trinitrobenzene may be due to the fact that the latent valencies of the oxygen atom are neutralised by the carbonyl in a manner similar to that suggested by Collie in dimethylpyrone.

We have previously pointed out (*Trans.*, 1910, **97**, 777) that compounds containing both hydroxyl and amino-groups do not form stable additive compounds with trinitrobenzene. We have not been able to confirm this by the examination of freezing-point curves, as mixtures of trinitrobenzene and an aminophenol decompose when heated. It is possible that the inability to form stable additive compounds may also be due to the fact that the subsidiary valencies of the oxygen and nitrogen atoms neutralise one another. This is supported by the readiness with which amines form additive compounds with phenols (compare Dale and Schorlemmer, *Trans.*, 1883, **43**, 185; Dyson, *ibid.*, 466; Hebebrand, *Ber.*, 1882, **15**, 1974; Philip, *Trans.*, 1903, **83**, 814; Philip and Smith, *ibid.*, 1905, **87**, 1733; Kremann, *Monatsh.*, 1906, **27**, 91; Dollinger, *ibid.*, 1910, **31**, 643; Schmidt and Wichmann, *Ber.*, 1891, **24**, 3237; Stevignon, *Bull. Soc. chim.*, 1910, [iv], **7**, 922), as do also phenols and ketones (Schmidlin and Lang, *Ber.*, 1910, **43**, 2806), and amines and quinones (Loring Jackson and Clarke, *Amer. Chem. J.*, 1905, **34**, 441).

Aromatic hydrocarbons also form additive compounds with trinitrobenzene. We have already prepared a number of these additive compounds. That formed by naphthalene and trinitrobenzene crystallises in light yellow-coloured needles, and the introduction of the hydroxyl group tends to deepen the colour of the additive compound. Other substituted derivatives of naphthalene also yield compounds with trinitrobenzene; thus, methyl- $\alpha$ -naphthoate and methyl- $\beta$ -naphthoate form stable additive compounds, which crystallise from alcohol in very pale yellow needles.

A few additive compounds of phenols with polynitro-derivatives of naphthalene, namely,  $\alpha$ -tri- and  $\beta$ -tetra-nitronaphthalene, have

## EXPERIMENTAL.

The following table shows the properties of the compounds prepared:

I.—*Additive Compounds of Phenols with Aromatic Poly-nitro-derivatives.*

Mols. of nitro- compound :	Components :	Formula.	Appearance.	Analysis.	
				M. p.	Found, per cent.
1 : 1	α-Naphthol and s-trinitro- benzene	C <sub>15</sub> H <sub>10</sub> O <sub>7</sub> N <sub>3</sub>	Orange-yellow needles	178—178°	N = 11.97
1 : 1	*β-Naphthol and s-trinitro- benzene	C <sub>16</sub> H <sub>11</sub> O <sub>7</sub> N <sub>3</sub>	{ Canary-yellow needles (alcohol) { Orange-yellow needles (benzene)}	158—158.5°	N = 11.65
1 : 1	Phenyl salicylate and s-tri- nitrobenzene	C <sub>9</sub> H <sub>8</sub> O <sub>9</sub> N <sub>3</sub>	Pale yellow needles	85°	N = 10.02
1 : 1	Benzyl salicylate and s-tri- nitrobenzene	C <sub>10</sub> H <sub>11</sub> O <sub>9</sub> N <sub>3</sub>	Pale yellow needles	89°	N = 12.89
2 : 1	Quinol disalicylate and s-tri- nitrobenzene	C <sub>20</sub> H <sub>18</sub> O <sub>9</sub> N <sub>6</sub>	Yellow prisms	170°	N = 11.23
2 : 1	+Methyl salicylate and s-tri- nitrobenzene	C <sub>21</sub> H <sub>20</sub> O <sub>9</sub> N <sub>6</sub>	Pale yellow, crystalline mass	about 80°	—
2 : 1	Pyrogallol and s-trinitrobenzene	C <sub>20</sub> H <sub>17</sub> O <sub>9</sub> N <sub>3</sub>	Canary-yellow, prismatic needles	163°	N = 12.84
2 : 1	2 : 7-Dihydroxyxanthophthaleine and s-trinitrobenzene	C <sub>12</sub> H <sub>10</sub> O <sub>9</sub> N <sub>3</sub>	{ Brown, transparent prisms (benzene) { Flat, brown plates (glacial acetic acid)}	162°	N = 11.11
—	Kalassium α-naphthoxide and s-trinitrobenzene	C <sub>16</sub> H <sub>11</sub> O <sub>9</sub> N <sub>3</sub>	Dark green precipitate	decomposed	—
1 : 1	1-Bromo-2-naphthol and s-tri- nitrobenzene	C <sub>16</sub> H <sub>10</sub> O <sub>7</sub> N <sub>3</sub> Br	Canary yellow needles	148°	Br = 18.1

Calcd.,

percent.

N = 11.77

N = 11.77

N = 11.65

N = 11.77

9.84

9.84

12.85

10.82

10.82

12.39

11.26

11.26

18.1

18.1

Components,	Mols. of nitro- compound : mols. of phenol.	Formula,	Appearance,	Analysis.	
				Found, per cent.	Calcd., per cent.
2 : 4-Dibromo-1-naphthol and α-trinitrobenzene	1 : 1	C <sub>16</sub> H <sub>9</sub> O <sub>7</sub> N <sub>3</sub> Br <sub>2</sub>	Yellow needles	Br = 30.5	31.06
*α, *β-tetrahydro-2-naphthol and α-trinitrobenzene	1 : 1	C <sub>16</sub> H <sub>11</sub> O <sub>7</sub> N <sub>3</sub>	Golden-yellow, prismatic needles		
*α, *β-tetrahydro-2-naphthol and α-trinitrobenzene	1 : 1	C <sub>16</sub> H <sub>13</sub> O <sub>8</sub> N <sub>3</sub>	Bright crimson needles	70°	—
Hydroxyquinoline and α-tri- nitrobenzene	1 : 1	C <sub>15</sub> H <sub>10</sub> O <sub>7</sub> N <sub>4</sub>	Sulphur-yellow needles	123.5—124	N = 15.73
Hydroxyquinoline and α-tri- nitrobenzene	1 : 2	C <sub>16</sub> H <sub>11</sub> O <sub>7</sub> N <sub>5</sub>	Greenish-yellow, lance-shaped prisms	199—200° (decomp.)	15.64
*β-Hydroxyquinoline and α-tri- nitrobenzene	1 : 1	C <sub>17</sub> H <sub>10</sub> O <sub>7</sub> N <sub>4</sub>	Brownish-yellow plates	193—195°	N = 13.9
Hydroxylepidine and α-tri- nitrobenzene	1 : 2	C <sub>20</sub> H <sub>12</sub> O <sub>8</sub> N <sub>5</sub>	Canary-yellow prisms	227—228°	N = 13.21
Hydroxy-2-methylquinolinolone and α-trinitrobenzene	1 : 1	C <sub>16</sub> H <sub>12</sub> O <sub>7</sub> N <sub>4</sub>	Canary-yellow, felted needles	200—201°	N = 14.34
*α-Naphthol and α-trinitro- naphthalene	1 : 1	C <sub>20</sub> H <sub>13</sub> O <sub>7</sub> N <sub>8</sub>	Brilliant red needles	117°	N = 10.54
*β-Naphthol and α-trinitro- naphthalene	1 : 1	C <sub>20</sub> H <sub>13</sub> O <sub>7</sub> N <sub>3</sub>	Orange-red needles	142°	N = 10.46
*β-Naphthol and α-trinitro- naphthalene	2 : 1	C <sub>20</sub> H <sub>18</sub> O <sub>7</sub> N <sub>6</sub>	Bright red prisms	148°	N = 12.77
*α-Naphthol and β-tetrano- toleum	1 : 1	C <sub>29</sub> H <sub>22</sub> O <sub>8</sub> N <sub>4</sub>	Scarlet needles	190—195° (decomp.)	N = 12.21
*β-Naphthol and β-tetrano- toleum	1 : 1	C <sub>29</sub> H <sub>22</sub> O <sub>9</sub> N <sub>4</sub>	Orange-yellow needles	190—200° (decomp.)	N = 12.33
*β-Naphthol and α-trinitro- tolueno	1 : 1	C <sub>17</sub> H <sub>13</sub> O <sub>7</sub> N <sub>3</sub>	Canary-yellow needles	110°	N = 11.33

III.—*Additive Compounds of Phenolic Filters with Aromatic Polynitro-derivatives.*

Mols. of nitro- compound :	Components,	Formula,	Appearance,	Analysis.	
				Found, per cent.	Calc., per cent.
*Cinnol dimethyl ether and *o-nitrotoluene	2 : 1	C <sub>10</sub> H <sub>6</sub> O <sub>2</sub> N <sub>6</sub>	Long, bright red prisms	M. p. 86.5°	N = 15.05 14.89
*Pyrogallal trimethyl ether *o-and <i>s</i> -nitrotoluene	1 : 1	C <sub>15</sub> H <sub>12</sub> O <sub>3</sub> N <sub>3</sub>	Flat, lustrous, bright yellow prisms	N = 11.06 11.02	
*Oxide dimethyl ether and *o-nitrotoluene	1 : 1	C <sub>16</sub> H <sub>12</sub> O <sub>3</sub> N <sub>3</sub>	Orange-yellow needles	N = 11.55 11.51	
Tyrosol and <i>s</i> -nitrotoluene	1 : 1	C <sub>12</sub> H <sub>10</sub> O <sub>3</sub> N <sub>3</sub>	Golden-yellow plates	76°	N = 11.15 11.17
*Safrole and <i>s</i> -nitrotoluene	1 : 1	C <sub>16</sub> H <sub>12</sub> O <sub>3</sub> N <sub>3</sub>	Golden-yellow plates	51°	{ trinitro- benzene = 56.8 }
Asarone and <i>s</i> -nitrotoluene	1 : 1	C <sub>16</sub> H <sub>12</sub> O <sub>3</sub> N <sub>3</sub>	Bright scarlet needles	85—86°	{ trinitro- benzene = 54.4 }
Asarone and 1,4-trinitrotoluene	1 : 1	C <sub>16</sub> H <sub>12</sub> O <sub>3</sub> N <sub>3</sub>	Orange-red plates	34—35°	N = 10.07 9.65
*Anisole and <i>s</i> -nitrotoluene	1 : 1	C <sub>9</sub> H <sub>10</sub> O <sub>2</sub> N <sub>8</sub>	Orange-red needles	67°	N = 9.66 9.65
*Asarole and <i>s</i> -nitrotoluene	1 : 1	C <sub>12</sub> H <sub>10</sub> O <sub>2</sub> N <sub>8</sub>	Bright scarlet plates	69—70°	—
*(o-Eugenyl methyl ether and *o-nitrotoluene)	1 : 1	C <sub>17</sub> H <sub>17</sub> O <sub>2</sub> N <sub>3</sub>	Deep prune needles (alcohol)	92.5°	N = 13.36 13.25
*Asarone and <i>s</i> -nitrotoluene	2 : 1	C <sub>14</sub> H <sub>12</sub> O <sub>3</sub> N <sub>6</sub>	Lighter prune, lustrous needles (benz. nr.)	77—78°	N = 10.12 10.00
Asarone and <i>s</i> -nitrotoluene	1 : 1	C <sub>18</sub> H <sub>12</sub> O <sub>3</sub> N <sub>3</sub>	Orange-red needles	109°	N = 10.87 10.71
2 : 4 : 6-Trinitroxyphenyl ketone and <i>s</i> -nitrotoluene	2 : 1	C <sub>22</sub> H <sub>12</sub> O <sub>6</sub> N <sub>6</sub>	Slender, canary-yellow needles	137—138°	N = 11.38 11.32
*Naphthyl methyl ether and <i>c</i> -nitrotoluene	1 : 1	C <sub>19</sub> H <sub>14</sub> O <sub>2</sub> N <sub>8</sub>	Sulphur-yellow needles	125.5°	N = 10.92 10.90
*Naphthyl ethyl ether and <i>s</i> -nitrotoluene	1 : 1	C <sub>21</sub> H <sub>16</sub> O <sub>2</sub> N <sub>8</sub>	Very yellow plates	112.5°	N = 9.76 9.70

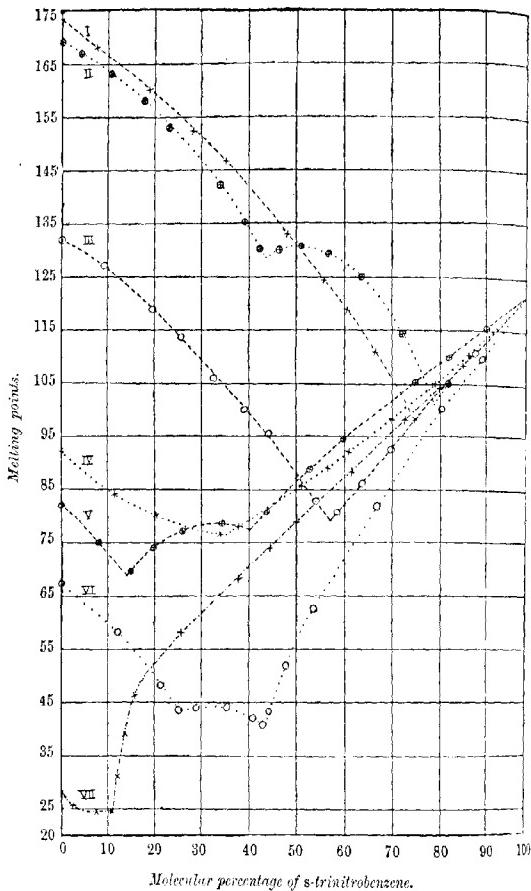
	Mols. of atom:	Components, nos. of phenol.	Formula.	Appearance.	M. P. °	Analyses.
$\beta$ -Naphthyl methyl ether and <i>s</i> -trinitrobenzene	1 : 1	$C_{17}H_{15}O_7N_3$	Long, canary-yellow needles	93.5°	N = 11.15	Calcd., per cent.
$\beta$ -Naphthyl ethyl ether and <i>s</i> -trinitrobenzene	1 : 1	$C_{18}H_{15}O_7N_3$	Pale canary-yellow needles	95°	N = 10.90	11.32
$\beta$ -Naphthyl phenyl ether and <i>s</i> -trinitrobenzene	2 : 1	$C_{28}H_{19}O_3N_6$	Bright lemon-yellow needles	105.5°	N = 12.95	10.90
$\beta$ -Naphthyl ether and <i>s</i> -tri- nitrobenzene	2 : 1	$C_{27}H_{20}O_3N_6$	Yellow plates	128°	N = 11.8	12.07
$\alpha$ -Dinitroxy-naphthalene	1 : 1	$C_{18}H_{12}O_8N_3$	Orange-yellow needles	111.5°	N = 10.57	10.47
* $\beta$ -Naphthyl ether and <i>s</i> -tri- nitrobenzene	1 : 1	$C_{27}H_{19}O_3N_6$	Light yellow, feathery needles	72°	N = 8.6	8.45
*Quinol dimethyl ether and <i>s</i> -trinitrotoluene	1 : 1	$C_{15}H_{13}O_7N_3$	Golden-brown, prismatic needles	45°	N = 11.74	11.51
*Pyrogallol trimethyl ether and <i>s</i> -trinitrotoluene	1 : 1	$C_{16}H_{17}O_7N_3$	Thick, dark yellow needles	56.5°	N = 10.57	10.63

### III.—Additive Compounds of Cyclic Oxygen Compounds with Aromatic Polynitro-derivatives.

Comarone and <i>s</i> -trinitro- benzene	1 : 1	$C_{14}H_9O_7N_3$	Long, flat, pale yellow plates	$103.5 - 104^{\circ}$	$\left\{ \begin{array}{l} \text{trinitro-} \\ \text{benzene} \\ = 61.9 \end{array} \right\}$	61.4
Diphenylene oxide and <i>s</i> -tri- nitrobenzene	1 : 1	$C_{18}H_{11}O_7N_3$	Lemon-yellow needles	96°	N = 11.12	11.02
$\alpha$ -Dimethylvinyl oxide and <i>s</i> -trinitrotoluene	1 : 1	$C_{20}H_{15}O_7N_3$	Slender, brownish needles	183.5°	N = 8.8	8.73

\* These compounds were prepared by using an excess of the phenol or phenolic ether. When the theoretical amounts of the components are used in the presence of alcohol or benzene as solvent, *s*-trinitrotoluene usually separates.

† These compounds were prepared by fusing the two components in the absence of a solvent, and are resolved into their components on the addition of a solvent.



Melting-point curves :

- I. s-Trinitrobenzene and xanthone.
- II. " " quinol.
- III. " " dimethylpyrone.
- IV. " " s-tribromophenol.
- V. " " fluorenone.
- VI. " " coumarin.
- VII. " " phenyl ether.

been prepared, and it is noticeable that the colours of these compounds are much more pronounced than those of the additive compounds of the same phenols with trinitrobenzene.

s-Trinitrotoluene also forms compounds with phenols and their derivatives, but on the whole they are less stable than the products derived from trinitrobenzene.

In several instances, melting-point curves have been constructed in order to determine whether there is combination between trinitrobenzene and certain oxygen compounds. By this method we have been able to show that dimethylpyrone, xanthone, s-tribromophenol, and phenyl ether do not form additive compounds, and that coumarin yields an excessively unstable product; fluorenone and quinol more stable compounds.

#### IV.—*Melting-point Curves.*

The seven curves given in the diagram show that the cyclic oxygen compounds, coumarin and fluorenone (diphenylene oxide), yield additive compounds with s-trinitrobenzene in the absence of a solvent, whereas xanthone and dimethylpyrone do not. Quinol also forms an additive compound, which is comparatively stable, but diphenyl ether and s-tribromophenol do not.

#### V.—*Non-formation of Additive Compounds.*

The following compounds do not appear to yield additive compounds with trinitrobenzene in the presence of a solvent: *p*-Hydroxyacetophenone, 2: 4-dihydroxybenzoic acid, and the isomeric 2: 5-dihydroxy-acid, quinic acid and its ester, triphenylcarbinol, *p*diphenol, diethylresorcinol, eugenol, eugenyl methyl ether, *p*-dihydroxydiphenylmethane, benzil, and benzoin.

In conclusion, we wish to thank Mr. F. Tutin for a specimen of 2: 4: 6-trimethoxyphenyl 3: 4-dimethoxystyryl ketone, and the Council of the Society for a grant which has covered part of the cost of this investigation.

EDWARD DAVIES CHEMICAL LABORATORIES,  
UNIVERSITY COLLEGE OF WALES,  
ABERYSTWYTH.

**XXVI.—The Relative Effect of Ethylenic and Acetylenic Linkings on Optical Rotatory Power.**

By THOMAS PERCY HILDITCH (1851 Exhibition Scholar).

THE study, by means of several series of esters and alkaloid salts, of the relative effects of ethylenic and acetylenic linkings on optical rotatory power has shown that Walden's simple rule that the rotatory power of the acetylenic member is intermediate between those of the saturated and ethenoid derivatives (*Zeitsch. physikal. Chem.*, 1896, **20**, 569) does not always hold good. Only two complete series of acids have, however, been used in this connexion— $\beta$ -phenylpropionic, cinnamic, and phenylpropionic acids, and succinic, fumaric, malic, and acetylenedicarboxylic acids. Further, in every instance so far observed, the ethylenic ester or salt shows an increase in rotatory power over the corresponding saturated compound, variations having appeared only in the relative effect of the acetylenic derivative. It is nevertheless probable that this consistent increase is due rather to the reinforcing effect of the contiguous carboxyl group than to the simple ethenoid radicle, for optically active compounds containing this grouping unconjugated with other unsaturated residues possess sometimes an enhanced and sometimes a diminished rotatory power:

	[M].	Difference.
Methyl $\alpha$ -propyl ether (Tschnigaeff, <i>J. Russ. Phys. Chem.</i> <i>Sov.</i> , 1902, <b>34</b> , 608)	- 182.5	..
Methyl allyl ether (Haller and March, <i>Compt. rend.</i> , 1904, <b>136</b> , 1695)	193.1	+ 10.6
$\alpha$ -Propyl santonate (Carnelutti and Nasini, <i>Ber.</i> , 1880, <b>13</b> , 2208)	+ 120.4	..
Allyl santonate (Carnelutti and Nasini, <i>Ber.</i> , 1880, <b>13</b> , 2208)	120.2	- 0.2
Tartarodi- $\alpha$ -propylamide (Frankland and Twiss, <i>Trans.</i> , 1906, <b>89</b> , 1852)	+ 290.0	—
Tarteradiallylamide (Frankland and Twiss, <i>Trans.</i> , 1906, <b>89</b> , 1852)	273.0	- 15.0

No similar active compound containing a simple acetylenic residue has apparently yet been prepared, but even when reinforced by the presence of an adjacent carboxyl group the effect of this linking is curiously uncertain. In two cases, indeed, the relative effects of the ethenoid and acetylenic groups appear to be determined by the solvent in which the polarimetric readings are made. For example, the author found that methyl phenylpropionate showed less rotatory power than either methyl cinnamate or methyl  $\beta$ -phenylpropionate in chloroform or acetone solutions (*Trans.*, 1908, **93**, 1), whilst Rupe (*Annalen*, 1909, **369**, 311) states that in benzene these esters conform to Walden's rule. Since the specimens used in the former

experiments furnished, when dissolved in benzene, numbers agreeing with those of Rupe, the discrepancy cannot be due to impurity or other experimental error in either case. The second example of this kind has occurred in the course of the work now being described.

The order of effect of unsaturation for amyl esters and coniine salts of the cinnamic series of acids is the same, but differs from that of salts of the more complicated alkaloids, brucine, codeine, or sinchonine (Trans., 1908, **93**, 700). It was thought that this might indicate that the rule was true for compounds of a simple optically active structure, and therefore the same esters of *d*-methylhexylcarbinol (*d*-*sec*-octyl alcohol) were prepared, and, in view of the experience with the methyl esters, were examined in chloroform and benzene, as well as in the liquid condition. Two distinct series of specimens (from different samples of active octyl alcohol) showed practically the same activity. The order observed was, however, not that anticipated, for, although the esters themselves just succeeded in conforming to the rule, the acetylenic compound possessed the greatest anomaly of the three in chloroform or benzene solution.\* The anomaly in rotatory power has been based, as usual, on the differences, "[D]\_n," from the mean molecular rotation of the higher fatty acid esters, and the data used in determining the latter "normal value" were as follows:

(a) *Without Solvent.*

	<i>d</i> 20°/4°.	[α] <sub>D</sub>	[M] <sub>D</sub>
<i>d</i> -Methylhexylcarbinol .....	0.8216	+ 9.57	+ 12.4
<i>d</i> -Methylhexylcarbinyl <i>n</i> -butyrate ...	0.8633	+ 8.20	+ 16.4
" " <i>n</i> -pentanoate ...	0.8580	8.58	18.3
" " <i>n</i> -hexoate .....	0.8562	8.43	19.2
Mean molecular rotation .....	—	—	+ 18.0

(b) *In Solution (2.5 per cent.).*

	Chloroform.		Benzene.	
	[α] <sub>D</sub>	[M] <sub>D</sub>	[α] <sub>D</sub>	[M] <sub>D</sub>
<i>d</i> -Methylhexylcarbinol .....	+ 8.76	+ 11.4	—	—
<i>d</i> -Methylhexylcarbinyl <i>n</i> -butyrate ....	+ 4.00	+ 8.00	+ 1.04	+ 2.08
" " <i>n</i> -pentanoate ....	3.72	7.96	0.96	2.05
" " <i>n</i> -hexoate .....	3.52	8.03	0.92	2.10
Mean molecular rotation.....	—	+ 8.0	—	+ 2.1

The values observed in the esters studied are collected in the next table.

\* It must be remarked that in all three cases the difference in [M]<sub>D</sub> between *d*-*sec*-octyl cinnamate and phenylpropionate is less than 1.5 per cent.

(a) *Without Solvent* (length of tube 0·1-dcm.; temperature 22°).

	$d^{20}/d^{\circ}$	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>
d-Methylhexylcarbinyl $\beta$ -phenylpropionate .....	0·9426	+11·92	+31·2	+13·9
" cinnamate .....	0·9645	35·32	91·8	73·8
" phenylpropionate .....	0·9876	35·08	90·5	72·5
"				

(b) *In Solution* (2·5 per cent.; length of tube 1·0-dcm.; temperature 22°).

	Chloroform.			Benzene.		
	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>
d-Methylhexylcarbinyl $\beta$ -phenylpropionate .....	+11·52	+30·2	+22·2	+6·00	+15·7	+13·7
d-Methylhexylcarbinyl cinnamate .....	30·40	79·1	71·1	33·04	85·9	85·9
d-Methylhexylcarbinyl phenylpropionate ...	30·88	79·7	71·7	35·12	90·6	85·9

The data derived from the succinic acid series has been based up to the present only on their alkaloidal salts, but the respective mono- and di-menthyl esters have now been prepared, and this survey of the relative effects of ethylenic and acetylenic groups on rotatory power will be concluded by quoting the figures so obtained. The measurements were made in chloroform and acetone solution at concentrations of about 5 and 2·5 per cent. Since concentration has little effect on the optical activity in these examples, it will suffice to give the results for one dilution only in each case; the temperature of measurement varied between 22° and 23·5°.

*Menthyl Hydrogen Esters: 2·0 per cent. solutions.*

	In chloroform.			In acetone.		
	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>
Succinate .....	-66·00	-169·0	+7·8	-65·50	-167·7	+6·3
Fumarate .....	71·25	189·9	19·7	69·25	175·9	11·7
Acetylenedicarboxylate ...	67·75	170·6	9·4	68·75	173·3	12·1

*Dimenthyl Esters: 2·5 per cent. solutions.*

	In chloroform.			In acetone.		
	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>
Succinate .....	-82·4	-324·6	+1·1	-81·4	-320·7	-0·8
Fumarate .....	100·6	394·3	36·0	99·4	389·6	+33·6
Acetylenedicarboxylate .....	84·2	328·4	8·0	85·6	333·9	5·8

The whole of the results now available may conveniently be summarised at this point:

Acid series.	Optically active system.	Solvent.	Rotatory power of:		
			Saturated.	Ethylenic.	Acetylenic.
Cinnamic, etc.	Amyl esters.*	—	Least.	Greatest.	Intermediate.
"	sec.-Octyl esters.	Benzene,	"	"	"
"	Menthyl esters, †	{ Chloroform }	"	"	"
Succinic, etc.	Methyl acid esters.	{ or acetone. }	"	"	"
"	Dimethyl esters.	Chloroform,	"	"	"
Cinnamic, etc.	Conine salts.	{ Chloroform }	"	"	"
"	sec.-Octyl esters.	{ or benzene. }	"	Intermediate.	Greatest.
"	Brucine salts.	Chloroform.	"	"	"
"	Cinchonine salts,	Codeine.	"	"	"
Succinic, etc.	Conine.	"	"	"	"
"	Cinchonine,	"	"	"	"
"	Codeine.	"	"	"	"
Cinnamic, etc.	Menthyl esters.	{ Chloroform }	Intermediate.	"	"
Succinic, etc.	Bornyl esters.	{ or acetone. }	Greatest.	Least.	
* Walden, <i>loc. cit.</i>	Brucine salts.	Chloroform.	"	Least.	Greatest.
+ Rupe, <i>loc. cit.</i>					

The most interesting points appear to be:

(a) There is no general rule to cover the relative effect of trebly- and doubly-linked carbon atoms.

(b) It is curious that in about half of the series examined the optical activity of the acetylenic compound approximates very nearly to that of either the saturated or the ethenoic derivative. This must, however, be attributed to coincidence, since it is sometimes the ethenoic and sometimes the saturated compound to which close resemblance is found.

(c) It would appear that, in addition to unsaturation, other factors must contribute powerfully to the total determinant of the rotatory power, and that whilst the influence of an ethenoic bond seems to be sufficiently strong to cause a uniform optical effect throughout, that of the acetylenic linking is less definite, and therefore more liable to be perturbed or masked by those due to other factors.

(d) The methyl esters of the cinnamic, etc., series manifest a different order in benzene solution to that in chloroform or acetone, and the sec.-octyl esters of the same acids give a different order when examined without solvent to that displayed when in chloroform or benzene solution.

(e) Derivatives of cinnamic and phenylpropionic acids show greater and better-defined anomalies than those of any of the other acids; in view of investigations on the effect of contiguous unsaturated groups on optical activity, this may safely be ascribed to the enhancing influence of the benzenoid residue in conjugation with the double or triple carbon linking.

## EXPERIMENTAL.

The active *d-methylhexylcarbinol* used was prepared from Kahlbaum's *sec.-octyl alcohol* (compare Pickard and Kenyon, *Trans., 1907, 91*, 2058). The sample finally used boiled at 86–87°/20 mm., and had  $D_4^{20}$  0·8216. The esters were made by heating equivalent quantities of the alcohol with the appropriate acid chloride at 190° for two or three hours, and, after other purification, were twice fractionated under diminished pressure before polarimetric examination; at Professor Guye's suggestion, the aliphatic compounds were analysed refractometrically as well as in the usual way (compare Guye and Jordan, *Bull. Soc. chim.*, 1896, [iii], 15, 474). All the esters were colourless, agreeably-smelling oils.

*d-Methylhexylcarbinyl n-butylate* boiled at 112°/20 mm.  $D_4^{20}$  0·8633,  $n_D^{20}$  1·41957, whence  $MR_D$  (found) = 58·57 (theory 58·84):

0·1027 gave 0·2711  $CO_2$  and 0·1129  $H_2O$ . C = 71·99; H = 12·22.  
 $C_{12}H_{24}O_2$  requires C = 72·00; H = 12·00 per cent.

*d-Methylhexylcarbinyl n-pentate* boiled at 116–117°/20 mm.  $D_4^{20}$  0·8580,  $n_D^{20}$  1·42287, whence  $MR_D$  (found) = 63·50 (theory, 63·41);  $D_4^{20}$  0·8562,  $n_D^{20}$  1·42547, whence  $MR_D$  (found) = 63·50 (theory, 63·41); 0·1153 gave 0·3066  $CO_2$  and 0·1300  $H_2O$ . C = 72·51; H = 12·53.

$C_{13}H_{26}O_2$  requires C = 72·90; H = 12·15 per cent.

*d-Methylhexylcarbinyl n-hexoate* boiled at 120–123°/20 mm.  $D_4^{20}$  0·8562,  $n_D^{20}$  1·42547, whence  $MR_D$  (found) = 68·30 (theory, 7·98); 0·0989 gave 0·2667  $CO_2$  and 0·1104  $H_2O$ . C = 73·53; H = 12·40.

$C_{14}H_{28}O_2$  requires C = 73·69; H = 12·28 per cent.

*d-Methylhexylcarbinyl β-phenylpropionate* boiled at 196–197°/20 mm.  $D_4^{20}$  0·9426,  $n_D^{20}$  1·47762, whence  $MR_D$  = 78·66:

0·1238 gave 0·3518  $CO_2$  and 0·1066  $H_2O$ . C = 77·50; H = 9·57.

$C_{17}H_{26}O_2$  requires C = 77·85; H = 9·92 per cent.

*d-Methylhexylcarbinyl cinnamate* boiled at 200°/25 mm.,  $D_4^{20}$  0·9645,  $n_D^{20}$  1·51451, whence  $MR_D$  = 81·22:

0·1203 gave 0·3444  $CO_2$  and 0·1020  $H_2O$ . C = 78·09; H = 9·42.

$C_{17}H_{26}O_2$  requires C = 78·45; H = 9·23 per cent.

*d-Methylhexylcarbinyl phenylpropiolate* boiled at 200–202°/25 mm.  $D_4^{20}$  0·9876,  $n_D^{20}$  1·51014, whence  $MR_D$  = 78·15:

0·1042 gave 0·3001  $CO_2$  and 0·0821  $H_2O$ . C = 78·56; H = 8·76.

$C_{17}H_{26}O_2$  requires C = 79·07; H = 8·53 per cent.

The monethyl esters of the succinic acid series were prepared by heating about 5 grams of the acid with 8 grams of menthol to a temperature of 120–130° in sealed tubes for ten hours. The ethereal solution of the reaction product was filtered and extracted twice or three times with sodium carbonate solution. The ethereal layer was dried and evaporated, and the residue quickly distilled

in a current of steam to remove any excess of the alcohol. The residue furnished the *dimenthyl* ester on re-extraction with ether.

The alkaline extract, containing the salts from unchanged acid and acid ester, was treated with dilute sulphuric acid, and extracted with ether, whereby the *hydrogen* ester was obtained. In this way fairly good yields of the succinates were obtained, but the results with the other two acids were not so good. Great difficulty was found in obtaining the latter esters in the solid state; indeed, this was not attained in the case of methyl hydrogen fumarate and dimethyl acetylenedicarboxylate. Since the esters could not be distilled in a vacuum without decomposition, recourse was had to the method of purification used in the case of the liquid alkyl hydrogen camphorates (Edminson and Hilditch, Trans., 1909, **97**, 225), after which the analytical numbers obtained agreed closely with those demanded by theory.

*Methyl hydrogen fumarate*,  $\text{CO}_2\text{H}\cdot\text{CH}=\text{CH}\cdot\text{CO}_2\cdot\text{C}_{10}\text{H}_{19}$ , is a colourless, viscous oil, not crystallising when cooled in a mixture of solid carbon dioxide and acetone, decomposing and charring at about  $200^\circ$ :

0·1826 gave 0·4400  $\text{CO}_2$  and 0·1514  $\text{H}_2\text{O}$ . C = 65·72; H = 9·21.

$\text{C}_{14}\text{H}_{22}\text{O}_4$  requires C = 66·14; H = 8·66 per cent.

*Dimenthyl fumarate*,  $\text{C}_{10}\text{H}_{19}\cdot\text{CO}_2\cdot\text{CH}=\text{CH}\cdot\text{CO}_2\cdot\text{C}_{10}\text{H}_{19}$ , crystallised in very large, colourless prisms, and was only obtained solid with great difficulty in the first instance, thereafter crystallising readily from light petroleum, and melting at  $55^\circ$ :

0·1938 gave 0·5200  $\text{CO}_2$  and 0·1810  $\text{H}_2\text{O}$ . C = 73·16; H = 10·38.

$\text{C}_{22}\text{H}_{40}\text{O}_4$  requires C = 73·47; H = 10·21 per cent.

*Methyl hydrogen acetylenedicarboxylate*,  $\text{CO}_2\text{H}\cdot\text{C}:\text{C}\cdot\text{CO}_2\cdot\text{C}_{10}\text{H}_{19}$ , crystallises in small, wax-like needles, melting at  $79^\circ$ :

0·1096 gave 0·2690  $\text{CO}_2$  and 0·0780  $\text{H}_2\text{O}$ . C = 66·92; H = 7·91.

$\text{C}_{14}\text{H}_{20}\text{O}_4$  requires C = 66·67; H = 7·94 per cent.

*Dimenthyl acetylenedicarboxylate*,  $\text{C}_{10}\text{H}_{19}\cdot\text{CO}_2\cdot\text{C}:\text{C}\cdot\text{CO}_2\cdot\text{C}_{10}\text{H}_{19}$ , is a colourless oil, not crystallising at the temperature of an acetone solution of solid carbon dioxide, and decomposing before boiling under diminished pressure (20 mm.):

0·1557 gave 0·4186  $\text{CO}_2$  and 0·0139  $\text{H}_2\text{O}$ . C = 73·31; H = 9·92.

$\text{C}_{24}\text{H}_{38}\text{O}_4$  requires C = 73·84; H = 9·74 per cent.

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**XXVII.—The Effect of Contiguous Unsaturated Groups on Optical Rotatory Power. Part VI. The Influence of the Carbonyl Group on Optical Rotatory Power. Part VII. The Relative Influences of Aromatic and Hydroaromatic Nuclei on Optical Rotatory Power. Part VIII. The Influence on Optical Activity of Two Contiguous Unsaturated Groups in Comparison with that of One Unsaturated Group at Varying Distances from the Optically Active Complex.**

By THOMAS PERCY HILDITCH (1851 Exhibition Scholar).

**PART VI.—The Influence of the Carbonyl Group on Optical Rotatory Power.**

THE work of Walden (*Zeitsch. physikal. Chem.*, 1896, **20**, 569), Ruge (*Annalen*, 1903, **327**, 157), Hartwall (*Diss., Helsingfors*, 1904), and the author (*Trans.*, 1908, **93**, 1, 700) has demonstrated that in general optically active esters and salts of acids containing an ethenoid group adjacent to the carboxyl group possess a greater degree of rotatory power than similar derivatives of the corresponding saturated acids. The present communication deals with an analogous series of compounds derived from ketonic acids, thus containing carbonyl in place of an ethenoid group in the above series.

The compounds chosen for the purposes of this investigation were the following:

Menthyl esters and brucine salts of glyoxylic, pyruvic, acetoacetic, and lœvulic acids.

Brucine salts of mesoxalic, oxalacetic, and acetonedicarboxylic acids.

Brucine salts of certain aromatic ketonic acids.

The measurements of rotatory power were carried out in dry chloroform solution and in general at two dilutions, 5 grams per 100 c.c. and 2·5 grams per 100 c.c. of solution respectively. The length of solution used was 2-dcm., and the temperature was maintained throughout at 20°. In the succeeding tables of results, there is given, in addition to the usual specific and molecular rotatory power, the "anomaly"  $[D]_D$  based on the difference between the molecular rotatory power of the compound in question and the

"normal value," that is, the mean molecular rotatory power of the esters or salts of the higher normal fatty acids with menthol or brucine, as the case may be (compare Trans., 1909, **95**, 1571).

### I.—Menthyl Esters of the Pyruvic Acid Series.

	C : 5.			C : 2:5.		
	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>
Menthyl pyruvate.....	-88°40	-188·5	+28·0	-82°00	-185·3	+24·1
(at once)	—	—	—	68°36	164·1	2·9
" acetoacetate .....	—	—	—	67°04	160·9	-0·3
" levulate .....	67°62	171·8	11·3	67°60	171·7	+10·5

Menthyl pyruvate and levulinic showed no appreciable mutarotation.

### II.—Brucine Salts of the Pyruvic Acid Series.

	C : 5.			C : 2:5.		
	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>
Brucine glyoxylate .....	-12·50	-60·7	+186·7	-12·62	-61·3	+190·7
" pyruvate .....	17·68	85·2	162·2	17·88	86·2	165·8
" acetoacetate .....	11·02	54·7	192·7	10·82	53·7	198·3
" levulate .....	34·40	175·5	71·9	34·88	177·9	74·1

### III.—Dibrucine Salts of the Mesoxalic Acid Series.

Brucine mesoxalate ...	-20·46	-189·1	+152·9	-20·70	-191·9	+156·1
" oxalacetate ...	39·40	362·4	66·2	38·80	357·0	73·5
" acetonedicarbonylate .....	45·84	428·2	33·3	45·84	428·2	37·9

### IV.—Brucine Salts of Aromatic Ketonic Acids.

Brucine benzoate .....	-25·10	-131·1	+116·3	-25·00	-129·0	+123·0
" phenylglyoxylate	6·00	32·6	214·8	6·14	33·4	218·6
" phenylpyruvate .....	+3·66	+20·4	267·8	+3·32	+18·5	270·5
" benzoylacetate .....	-32·26	-180·0	67·4	-33·83	-188·8	63·2
" benzylpyruvate .....	9·59*	54·9*	192·5	9·81*	53·5*	196·5
" <i>B</i> -benzoylpropiolate .....	32·18	184·1	63·3	31·88	182·4	69·6
" benzoylpyruvate .....	+10·26	+60·1	307·5	+11·28	+66·1	318·1

\* C : 4·32 and 2·16 respectively.

It will be seen that this system—carbonyl-carboxyl—follows in its main outlines the same rule as the other conjugated structures examined, the anomalies, prominent in those members containing the unsaturated residues adjacent to each other, rapidly declining as the latter are separated. One or two points, however, require special remark:

(a) One cannot always be certain that the carbonyl group is always present as such, since there frequently exists the possibility of an enolic structure in this part of the molecule.

(b) The carbonyl groups in glyoxylic and mesoxalic acids are modified by the addition of a molecule of water, thus lessening the total amount of residual affinity and to a certain extent invalidating the comparison. Consequently, if it be granted from the other examples that the carbonyl-carboxyl grouping enhances optical activity, the true anomalies in these two cases would be somewhat higher.

The series of aromatic ketonic acid salts is especially instructive, for in addition to confirming the general results arrived at from the aliphatic keto-acids, it further demonstrates that:

(a) The carbonyl group alone, when adjacent to the carboxyl group, creates an effect almost as pronounced as that of the benzoyl radicle (phenylpyruvic, benzylpyruvic acids).

(b) The benzoyl system, when separated by methylene groups from the asymmetric part of the molecule, ceases to a great extent to influence the activity (benzoylacetic and  $\beta$ -benzoylpropionic acids).

(c) The benzoyl system, accompanied in the same molecule by a conjugate carbonyl-carboxyl group, produces the maximum effect.

It therefore appears that the carbonyl group, like various other unsaturated groups, causes anomalies in molecular rotatory power; quantitatively speaking, the polarimetric effect of the carbonyl group is probably somewhat less than that of an ethenoid residue under similar conditions. On the other hand, adjacent carbonyl and carboxyl groups together exert an influence on optical activity comparable to that displayed by a benzoyl radicle—a system possessed of considerable residual affinity.

Finally, either by separating the adjacent unsaturated groups or by removing the conjugated system en bloc away from the optically active complex, the anomaly in optical rotatory power may be much diminished or even caused to disappear.

#### PART VII.—*The Relative Influences of Aromatic and Hyperaromatic Nuclei on Optical Rotatory Power.*

Although no fresh physical evidence as to the absolute structural condition of the "benzene ring" is yet available from the rotatory power of optically active aromatic compounds, one may conclude from the values given by Rupe and his students (*loc. cit.*) for certain menthyl esters of hydroaromatic acids that the successive

introduction of ethylenic bonds, culminating finally in an aromatic nucleus, progressively increases optical activity:

	[M] <sub>D</sub>	[D] <sub>D</sub>
Methyl cyclohexanecarboxylate .....	-157.2	-3.3
" $\Delta^1$ -cyclohexenecarboxylate .....	197.0	+36.5
" benzoate.....	217.2	56.7
" $\Delta^1$ -ac-tetrahydro- $\alpha$ -naphthoate ...	-215.6	+55.1
" $\alpha$ -naphthoate .....	245.3	84.8

There is, however, nothing to show whether the maximum influence of the phenyl group is due to three conjugated ethylenic bonds or to the residual affinity of the radicle as a whole, and accordingly for the purpose of the present paper the benzenoid residue is regarded as a single unsaturated group.

Some experiments, which incidentally illustrate the conditions under which ring-formation affects optical activity, have been carried out by the author to determine the nature of the influence of the aromatic residue from the rotatory powers of salts of various corresponding aromatic and hydroaromatic bases with some optically active acids.

The solutions designed for measurement in the polariscope were made up from the accurately weighed requisite amounts of the base and acid concerned, and the salts formed were subsequently recovered for analysis, etc.

The acids chosen were *d*-camphoric, *d*-camphor- $\pi$ -sulphonic, and *d*-tartaric; the use of chloroform as a solvent, which is particularly desirable in the case of salts owing to its non-hydroxyllic nature, was precluded in the salts of camphoric and tartaric acids by reason of insolubility. Consequently it was necessary to use alcohol for the camphorates, and water for the tartrates. The presence of an ionising solvent introduces a conflicting influence—the constant "molecular" rotation of ions (Oudemans-Landolt law); nevertheless, probably in consequence of incomplete dissociation, differences were found of the same qualitative nature as those manifested in the case of the camphor- $\pi$ -sulphonates.

In order to obtain a basis for the approximate numerical estimation of anomalies, it was desirable to ascertain the molecular rotatory power of salts of these acids with the normal aliphatic amines.

Since the volatility of the lowest members of the fatty amines rendered them difficult to manipulate in these experiments, whilst the higher members are difficult to obtain, the molecular rotatory power of the *n*-butylamine salts of the acids employed was accepted as an approximate series constant (Tschugaeff, *Ber.*, 1898, **31**, 360,

1775; Hilditch, Trans., 1909, **95**, 1571), and the following values were thus obtained:

Solvent.	C : 5 per cent.			C : 5 per cent.		
	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>
Camphoric acid.....	Alcohol	+48.02	+96.0	+47.72	+95.1	
Di- <i>n</i> -butylamine camphorate.....	"	+10.96	+37.9	+11.16	+35.8	
Camphor- $\pi$ -sulphonic acid.....	Chloroform	+24.82	+57.6	+24.04	+55.6	
<i>n</i> -Butylamine camphor- $\pi$ -sulphonate.....	"	+20.36	+62.1	+20.44	+62.3	
Tartaric acid.....	Water	+14.02	+21.0	+14.44	+21.7	
Di- <i>n</i> -butylamine tartrate .....	"	+17.86	+52.9	+17.40	+51.5	

The following tables show the polarimetric results derived from the various salts studied:

### I.—Neutral Camphorates in Alcohol.

Base.	C : 5 per cent.			C : 2.5 per cent.		
	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>
Aniline .....	+32.50	+125.4	+87.5	+31.84	+122.9	+84.3
Pyridine .....	25.90	92.7	54.8	27.12	97.1	58.5
Piperidine .....	14.24	52.7	14.8	14.36	53.1	14.3
Quinoline .....	+19.16	+87.7	+49.8	+18.76	+85.9	+47.2
Tetrahydroquinoline .....	17.56	81.8	44.9	17.28	80.5	41.8
<i>a</i> -Naphthylamine .....	+18.12	+88.1	+50.2	+18.00	+87.5	+48.6
<i>ar</i> -Tetrahydro- <i>a</i> -naphthylamine .....	16.92	83.6	45.7	16.76	82.8	41.2
<i>b</i> -Naphthylamine .....	+18.61	+90.6	+52.7	+18.72	+91.0	+49.4
<i>ac</i> -Tetrahydro- <i>b</i> -naphthylamine .....	14.38	71.0	33.1	14.32	70.7	32.1

### II.—Camphor- $\pi$ -sulphonates in Chloroform.

Base.	C : 5 per cent.			C : 2.5 per cent.		
	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>
Aniline .....	+23.28	+75.7	+13.6	+23.32	+75.8	+13.5
Pyridine .....	31.42	97.7	35.6	31.72	98.7	36.4
Piperidine .....	22.94	72.7	10.6	21.40	67.8	5.3
Quinoline .....	+27.90	+100.7	+38.6	+26.96	+97.3	+35.1
Tetrahydroquinoline .....	25.98	94.8	32.7	25.36	92.0	30.3
<i>a</i> -Naphthylamine .....	+21.38	+80.2	+18.1	+20.92	+78.4	+18.1
<i>ar</i> -Tetrahydro- <i>a</i> -naphthylamine .....	19.92	75.5	13.4	19.80	75.0	12.7
<i>b</i> -Naphthylamine .....	+21.54	+80.8	+18.7	+20.80	+78.0	+18.7
<i>ac</i> -Tetrahydro- <i>b</i> -naphthylamine .....	17.36	65.8	3.7	17.36	65.8	3.5

III.—*Neutral Tartrates in Water.*

Base.	C : 5 per cent.			C : 2·5 per cent.		
	[α] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>	[α] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>
Aniline .....	+16·58	+55·7	+2·8	+16·12	+54·2	+2·7
Pyridine .....	19·30	59·5	6·6	18·72	57·7	6·2
Piperidine .....	17·12	54·8	1·9	16·80	53·8	2·3
Quinoline .....	+13·22	+54·0	+1·2	+12·80	+52·2	+0·7
Tetrahydroquinoline .....	13·42	55·8	2·9	12·80	53·3	1·8

The anomalies in the diquinoline tartrate group are not outside the limits of experimental error, and it was impossible to employ the naphthylamine tartrates on account of their sparing solubility.

Analysing these results (which, it must be conceded, are, for optical activity, remarkably consistent), we have:

Base.	Constitution.	Anomaly shown in rotatory power.
(a) Aniline.	Benzoid conjugated with amino-group.	Well defined.
Pyridine.	Benzoid group.	Well defined.
Piperidine.	Alicyclic group.	Relatively small.
(b) Quinoline.	Two conjugated aromatic nuclei.	Well defined.
Tetrahydroquinoline.	Aromatic system + alicyclic amine, the former being also adjacent to the secondary amino-group.	Almost as pronounced as that due to quinoline.
(c) α-Naphthylamine.	Amino-group adjacent to two conjugated aromatic nuclei.	Well defined.
α-Tetrahydro-α-naphthylamine.	Alicyclic + benzoid systems, the latter still contiguous to the amino-group.	Slightly less than with α-naphthylamine.
(d) β-Naphthylamine.	Similar to α-naphthylamine.	Much the same as α-naphthylamine.
β-Tetrahydro-β-naphthylamine.	Alicyclic + benzoid systems, the latter separated by the former from the amino group.	Relatively small.

The whole series therefore shows very clearly the enhancing effect of an aromatic group as contrasted with the very small effect of a hydroaromatic nucleus. The only other instance of reduced naphthylamine derivatives (which are obviously exceptionally suited for this comparison) is exactly parallel (Frankland and Ormerod, Trans., 1903, **83**, 1342):

	[M] <sub>D</sub>
Tartarodi-β-naphthylamide .....	+1163
Tartarodi-α <sub>c</sub> -tetrahydro-β-naphthylamide .....	840
Tartarodi-α <sub>c</sub> -tetrahydro-β-naphthylamide.....	240

These results show that a benzenoid group, when united to another unsaturated group, enhances optical activity, and that the preponderating factor is its unsaturated nature, its ring-structure having very little to do with its influence on rotatory power.

It is frequently stated that ring-formation usually profoundly alters the rotation of a substance, but a brief examination of the literature will reveal that, while this is very true when the asymmetric atoms themselves take part in the formation of the ring system, in all other cases corresponding open- and closed-chain compounds show only small and indefinite changes.

By way of example, and in addition to the results above, we may quote those of Rupe (*loc. cit.*):

	[M] <sub>D</sub>	[M] <sub>L</sub>		[M] <sub>D</sub>	[M] <sub>L</sub>	
Menthyl cyclopropanecarboxylate.....	- 153·5	- 164·7	Menthyl <i>n</i> -butyrate,			
"      cyclopentane carboxylate .....	164·4	165·7	"      " - <i>n</i> -valerate,			
"      cyclopentane carboxylate.....	171·3	164·7	"      " - <i>n</i> -hexanoate,			
"      cyclohexane carboxylate .....	157·2	165·9	"      " - <i>n</i> -heptanoate,			

PART VIII.—*The Influence on Optical Activity of Two Contiguous Unsaturated Groups in Comparison with that of One Unsaturated Group at Varying Distances from the Optically Active Complex.*

Attention was drawn by Tschugaeff (*loc. cit.*) to the rotatory power of the first three members of menthyl esters of the homologous phenyl aliphatic acids and to those of the corresponding amyl esters (Guye and Chavanne, *Bull. Soc. chim.*, 1896, [iii], 15, 177), pointing out that the value in both, abnormally large in the benzoates, decreased to almost the average value of esters of a normal aliphatic acid when the third member was reached:

Ester.	Anhyd.		Menthyl.	
	[M] <sub>D</sub>	[D] <sub>L</sub>	[M] <sub>D</sub>	[D] <sub>L</sub>
Mean value of fatty acid ester .....	+ 4·33	-	- 157·8	-
Benzal .....	+ 9·52	+ 5·19	- 236·3	+ 78·5
Phenylacetate .....	7·91	3·58	190·7	32·9
<i>β</i> -Phenylpropionate .....	4·73	0·40	161·9	4·7

The brucine and cinchonine salts of the same acids, more recently examined by the author (*Trans.*, 1908, 93, 1388), show the same gradation in optical anomaly.

Tschugaeff concluded that the power of an unsaturated group to affect optical activity rapidly declined as it was separated from the asymmetric system, and Guye (*Proc.*, 1901, 17, 48) adopted these examples as particular cases of his more general conclusion that substitution at a point sufficiently removed from the asymmetric atom creates little optical effect.

Rupe (*loc. cit.*) elaborated the question by his work on isomeric pentenoic and hexenoic menthyl esters, and suggested that the size

of the anomaly produced by unsaturation is determined mainly by the proximity of the unsaturated group to the asymmetric system:

	[M] <sub>D</sub>
Menthyl $\Delta^{\alpha\beta}$ -pentenoate .....	-177.1
" $\Delta^{\gamma\gamma}$ -pentenoate .....	172.5
" $\Delta^{\delta\delta}$ -pentenoate .....	160.2
" $\Delta^{\alpha\beta}$ -hexenoate .....	-172.4
" $\Delta^{\gamma\gamma}$ -hexenoate .....	161.1
" $\Delta^{\delta\delta}$ -hexenoate .....	153.5
" $\Delta^{\beta\epsilon}$ -hexenoate .....	151.4

The author has in previous papers (Trans., 1909, **95**, 336, 1570, etc.) attributed many cases of abnormal rotatory power to the presence of adjacent or "conjugated" unsaturated systems in the molecules in question, and it appears well to discuss in detail those cases which are at first sight equally well covered either by the latter or by the Tschugaeff-Rupe explanation. For it must be observed that in the examples from which these authors' deductions are made, a carboxyl residue always intervenes between the phenyl and asymmetric radicles, and thus, simultaneously with increasing distance of the phenyl group from the asymmetric system, the contiguity of the unsaturated phenyl and carboxyl residues is automatically destroyed.

It is interesting in this connexion to notice that in the case of some neutral aniline and benzylamine salts of optically active acids, in which the benzenoid and carboxyl residues are separated by a (saturated) quinquevalent nitrogen atom, the decrease in optical activity is not always so marked as in the former instances of simple aromatic esters and salts. These examples, which were observed under the same conditions as the similar salts described on a preceding page, are collected in the next table.

Acid.	Solvent.	Percentage concentra-	Aniline salt.			Benzylamine salt.		
			[a] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>	[a] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>
Camphoric	Alcohol	5.0	+32.50	+125.4	+87.5	+16.92	+70.0	+32.1
	"	2.5	31.84	122.9	84.3	17.16	71.0	32.4
Camphor- $\pi$ -sulphonic	Chloroform	5.0	+23.28	+75.7	+13.6	+22.00	+74.6	+12.5
	"	2.5	28.32	75.8	13.5	21.36	72.4	10.1
Tartaric	Water	5.0	+10.58	+55.7	+2.8	+18.28	+66.5	+18.7
	"	2.5	16.12	54.2	2.7	17.40	63.3	11.8

If, on the other hand, compounds are selected in which it is possible, while maintaining the same relative positions of unsaturated groups to asymmetric system, to alter the amount of residual affinity (and therefore of any effect due to conjugation) by changing the character of one of the unsaturated radicles, the results obtained are very different. In some cases, for example,

one can compare corresponding benzyl and benzoyl derivatives of an active substance, when, whilst the phenyl group is left at the same distance from the active complex, there is in one case a single phenyl group and in the other a conjugated (phenyl+carbonyl) system.

We may thus compare some ethers of menthol described by Tschugaeff (*J. Russ. Phys. Chem. Soc.*, 1902, **34**, 606) with the esters to which reference has already been made:

	[M] <sub>o</sub>	Difference.
Menthyl ethyl ether, $\text{CH}_3\text{CH}_2\text{O}'\text{C}_{10}\text{H}_{19}$ .....	- 179°	
Menthyl benzyl ether, $\text{C}_6\text{H}_5\text{CH}_2\text{O}'\text{C}_{10}\text{H}_{19}$ .....	- 232° 7	53·7
Menthyl acetate, $\text{CH}_3\text{CO}'\text{O}'\text{C}_{10}\text{H}_{19}$ .....	- 157° 3	
Menthyl benzoate, $\text{C}_6\text{H}_5\text{CO}'\text{O}'\text{C}_{10}\text{H}_{19}$ .....	- 236° 3	79·0

A similar comparison of the corresponding amyl ethers and esters (Guye and Chavanne, *loc. cit.*) leads to the same result:

	[M] <sub>o</sub>	Difference.
1-Amyl ethyl ether, $\text{CH}_3\text{CH}_2\text{O}'\text{C}_5\text{H}_{11}$ .....	+ 0° 7	
1-Amyl benzyl ether, $\text{C}_6\text{H}_5\text{CH}_2\text{O}'\text{C}_5\text{H}_{11}$ .....	+ 3° 2	2·5
1-Amyl acetate, $\text{CH}_3\text{CO}'\text{O}'\text{C}_5\text{H}_{11}$ .....	+ 3° 3	
1-Amyl benzoate, $\text{C}_6\text{H}_5\text{CO}'\text{O}'\text{C}_5\text{H}_{11}$ .....	+ 9° 6	6·3

Both these cases involve change of residual affinity without any relative change of molecular position, and all show differences in rotatory power quite as marked as in the first-mentioned series, which involve progressive removal of an unsaturated radicle. Moreover, the examples of menthyl and amyl ethers display unmistakably the peculiar anomaly produced by conjugation, apart from any question of relative position in space.

It has been remarked (Trans., 1908, **93**, 1618) that the sulphonic group  $\text{SO}_2$  behaves as a relatively saturated group with reference to optical activity; use has been made of this fact to produce another series of comparisons bearing upon the present subject, in which, again without altering relative molecular positions, a conjugated system XY has been changed by replacing one member of the system (Y:CO) by another of less residual affinity (Y: $\text{SO}_2$ ), rather than by an almost completely saturated group (Y: $\text{CH}_2$ ), as in the last examples. As the details given below demonstrate, in all cases the effect on optical activity is greatest in presence of the most unsaturated conjugated system, and when more than two systems are compared, the optical anomaly falls off in the same order as the residual affinities of the systems concerned.

The compounds studied in this way include, on the one hand, corresponding arylcarboxylic and arylsulphonic esters of menthol, and, on the other, the acetyl, benzoyl, and benzenesulphonyl derivatives of cinchonine and of cinchonidine.

The polarimetric measurements were carried out in chloroform solutions in a 2-dcm. tube maintained at a temperature of 13–14°.

Observations were made in the case of the menthyl esters with solutions containing 5 and 2·5 grains per 100 c.c. of solution respectively, and with solutions of 2 per cent. concentration of the alkaloidal derivatives. The results are summarised in the following tables:

### I.—Menthyl Esters.

Ester.	C : 5.			C : 2·5.		
	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	[D] <sub>D</sub>
Benzoate.....	- 85·60	- 222·6	+ 62·1	- 86·04	- 223·8	+ 62·6
Benzenesulphonate .....	72·68	215·1	54·6	73·20	216·7	55·5
<i>p</i> -Toluatesulphonate.....	- 95·22	- 260·9	+ 100·5	- 95·36	- 261·3	+ 100·1
<i>p</i> -Toluenesulphonate.....	66·76	206·9	46·4	66·80	207·1	45·9
<i>β</i> -Naphthoate.....	- 90·60	- 280·9	+ 120·4	- 91·12	- 282·5	+ 121·3
Naphthalene- <i>β</i> -sulphonate.	56·50	195·4	31·9	57·12	197·6	36·4

### II.—Cinchonine Derivatives.

Substituent.	C : 2.		
	[ $\alpha$ ] <sub>D</sub>	[M] <sub>D</sub>	Difference.
Acetyl.....	+ 108·50	+ 364·6	—
Benzenesulphonyl .....	+ 62·15	+ 269·7	- 94·9
Benzoyl .....	- 27·80	- 110·6	- 475·2

### III.—Cinchonidine Derivatives.

Acetyl.....	+ 12·90	+ 43·3	—
Benzenesulphonyl .....	+ 11·43	+ 49·6	+ 6·3
Benzoyl .....	+ 98·65	+ 392·6	+ 349·3

The conclusion is therefore reached that, in compounds where the influence of two or more given radicles on optical activity may be due either to their proximity to the asymmetric nucleus or to conjugated unsaturation, both causes contribute to the effect, but conjugation is evidently the predominating factor.

The series of brucine salts of aromatic ketonic acids given on a preceding page forms an excellent example of the combined effects of conjugation and of varying degrees of proximity of the unsaturated systems to the optically active group. Thus, when the acid group  $\text{CO}_2\text{H}$  remains attached to a carbonyl group, the anomaly is uniformly high, and is but slightly altered by successive removal of the phenyl group to more remote parts of the molecule, whilst the maximum exaltation occurs when there are two sets of conjugated systems in the molecule, although one of these is relatively distant from the asymmetric complex:

Brucine salt of:	[M] <sub>D</sub>	[D] <sub>D</sub>
Phenylglyoxylic acid, $\text{C}_6\text{H}_5\text{CO}(\text{CO}_2\text{H})$ .....	- 32·6	+ 214·8
Phenylpyruvic " $\text{C}_6\text{H}_5\text{CH}_2\text{CO}(\text{CO}_2\text{H})$ .....	+ 29·4	267·8
Benzylpyruvic " $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CO}(\text{CO}_2\text{H})$ .....	- 54·9	192·5
Benzoylpyruvic " $\text{C}_6\text{H}_5\text{COCH}_2\text{CO}(\text{CO}_2\text{H})$ .....	+ 60·1	307·5

On the other hand, Rupe's explanation is plainly supported by those salts wherein the conjugated system  $C_6H_5\cdot CO$  is itself progressively separated from the optically active part of the molecule.

For instance, brucine  $\beta$ -phenylpropionate has an anomaly of 39·7, whilst that of the  $\beta$ -benzoylpropionate is 63·3:

Brucine salt of :	[M] <sub>n</sub>	[D] <sub>n</sub>
Phenylglyoxylic acid, $C_6H_5\cdot CO\cdot CO_2H$ .....	-32·6	+21·8
Benzoylacetic , , $C_6H_5\cdot CO\cdot CH_2\cdot CO_2H$ .....	180·0	67·4
$\beta$ -Benzoylpropionic acid, $C_6H_5\cdot CO\cdot CH_2\cdot CH_2\cdot CO_2H$ .....	184·1	63·3

#### EXPERIMENTAL.

*Menthyl pyruvate, acetoacetate, and laevulinate* have already been described by Cohen and Whately (Trans., 1901, **79**, 1309), Lapworth and Hann (Trans., 1902, **81**, 1479), and McKenzie (Trans., 1905, **87**, 1380), but in order that all three might be examined under identical polarimetric conditions their preparation was repeated. The author's specimens possessed physical properties agreeing with those described by the above authors, and furnished satisfactory analytical numbers.

The brucine salts, except in a few stated cases, were directly made up from the equivalent amounts, accurately weighed, of the pure alkaloid and acid, dissolved in the corresponding quantity of chloroform, and then measured in the polariscope, after which they were recovered, crystallised, and analysed.

*Brucine glyoxylate*,  $C_3H_4O_4, C_{28}H_{26}O_4N_2, 4H_2O$ , was prepared by mixing roughly equivalent quantities of the acid (prepared as described by Perkin and Dupper, Trans., 1868, **21**, 197) and base in alcohol, precipitating by ether, and finally crystallising from a mixture of ether and alcohol. It formed a cream, micro-crystalline powder, which frothed at 160°, and decomposed at about 200°:

0·1049 gave 0·2083  $CO_2$  and 0·0634  $H_2O$ . C=54·14; H=6·93.

$C_{25}H_{30}O_4N_2, 4H_2O$  requires C=53·76; H=6·81 per cent.

*Brucine Pyruvate*,  $C_3H_4O_3, C_{28}H_{26}O_4N_2, 3H_2O$ .—Soft, cream-coloured crystals, readily soluble in water, melting at 85°, and evolving  $H_2O$  at 105—110°:

0·1417 gave 0·3028  $CO_2$  and 0·0895  $H_2O$ . C=58·28; H=7·01.

$C_{26}H_{30}O_7N_2, 3H_2O$  requires C=58·21; H=7·09 per cent.

*Brucine acetoneacetate*,  $C_4H_6O_3, C_{28}H_{26}O_4N_2, 4H_2O$ , was prepared from the sodium salt of the acid and brucine hydrochloride in absolute alcohol, subsequently crystallising from a mixture of ether and alcohol. It appeared as a white, soft, crystalline powder, partly melting at 147—150°:

0·1880 gave 0·3950  $CO_2$  and 0·1178  $H_2O$ . C=57·30; H=6·96.

$C_{27}H_{32}O_7N_2, 4H_2O$  requires C=57·04; H=7·04 per cent.

*Brurine Laevulate*,  $C_5H_8O_3C_{23}H_{26}O_4N_2.4H_2O$ .—Very small, hard, white crystals, which melt sharply at  $58^\circ$ , froth up violently at  $112-114^\circ$ , and again leave a clear liquid:

01344 gave 0·2854 CO<sub>2</sub> and 0·0737 H<sub>2</sub>O. C=57·91; H=7·32.

$C_{28}H_{31}O_7N_2.4H_2O$  requires C=57·73; H=7·22 per cent.

*Dibrucine Mesoxalate*,  $C_3H_4O_6(C_{23}H_{26}O_4N_2)_2$ .—A white, crystalline powder, showing no change in appearance below  $250^\circ$ :

01020 gave 0·2386 CO<sub>2</sub> and 0·0583 H<sub>2</sub>O. C=63·80; H=6·36.

$C_{49}H_{56}O_{14}N_4$  requires C=63·63; H=6·06 per cent.

*Dibrucine Oxalacetate*,  $C_4H_4O_5(C_{23}H_{26}O_4N_2)_2.2H_2O$ .—Soft, white nodules from ethyl acetate, melting with much frothing at  $163-166^\circ$ :

01596 gave 0·3687 CO<sub>2</sub> and 0·0988 H<sub>2</sub>O. C=62·98; H=6·88.

$C_{50}H_{56}O_{13}N_4.2H_2O$  requires C=62·76; H=6·28 per cent.

*Dibrucine acetonedicarboxylate*,  $C_5H_6O_9(C_{23}H_{26}O_4N_2)_2.H_2O$ , separates from benzene in large, transparent, cubical crystals, melting at  $179-180^\circ$ :

01551 gave 0·3655 CO<sub>2</sub> and 0·0905 H<sub>2</sub>O. C=64·27; H=6·48.

$C_{51}H_{55}O_{13}N_4.H_2O$  requires C=64·29; N=6·30 per cent.

The necessary aromatic ketonic acids were obtained by methods devised by Claisen (*Ber.*, 1887, **20**, 655, 2196; 1888, **21**, 1131), Erlenmeyer (*Annalen*, 1892, **271**, 163), Perkin (*Trans.*, 1884, **45**, 178), and Fittig (*Ber.*, 1896, **29**, 2582), and the purity of each was controlled by determination of the melting point.

*Brucine Phenylglyoxylate*,  $C_8H_6O_3C_{23}H_{26}O_4N_2.H_2O$ .—Colourless, stable crystals, by ethereal precipitation of the alcoholic solution; the salt decomposes, but does not melt at  $230^\circ$ :

01112 gave 0·2697 CO<sub>2</sub> and 0·0636 H<sub>2</sub>O. C=66·15; H=6·36.

$C_{31}H_{28}O_7N_2.H_2O$  requires C=66·19; H=6·05 per cent.

*Brucine Phenylpyruvate*,  $C_9H_8O_3.C_{23}H_{26}O_4N_2.2\frac{1}{2}H_2O$ .—A cream-coloured salt, melting and decomposing at  $182-183^\circ$ :

01190 gave 0·2774 CO<sub>2</sub> and 0·0685 H<sub>2</sub>O. C=63·57; H=6·40.

$C_{32}H_{29}O_7N_2.2\frac{1}{2}H_2O$  requires C=63·68; H=6·46 per cent.

*Brucine Benzylacetate*,  $C_9H_{10}O_3C_{23}H_{26}O_4N_2.5\frac{1}{2}H_2O$ .—Colourless, slender needles, readily soluble in water, melting and decomposing at  $196^\circ$ :

01216 gave 0·2600 CO<sub>2</sub> and 0·0776 H<sub>2</sub>O. C=58·30; H=7·09.

$C_{33}H_{29}O_7N_2.5\frac{1}{2}H_2O$  requires C=58·43; H=6·85 per cent.

*Brucine Benzylpyruvate*,  $C_{10}H_{10}O_3C_{23}H_{26}O_4N_2.5H_2O$ .—A colourless, crystalline powder, melting at  $100-103^\circ$ :

01093 gave 0·2405 CO<sub>2</sub> and 0·0670 H<sub>2</sub>O. C=60·01; H=6·81.

$C_{33}H_{30}O_7N_2.5H_2O$  requires C=59·81; H=6·95 per cent.

*Brucine  $\beta$ -Benzoylpropionate*,  $C_{10}H_{10}O_3C_{23}H_{26}O_4N_2 \cdot 3H_2O$ . — A cream-coloured, deliquescent, micro-crystalline powder, evolving water, and fusing at  $101-103^\circ$ :

0·1071 gave 0·2472  $CO_2$  and 0·0660  $H_2O$ . C = 62·94; H = 6·85.  
 $C_{33}H_{34}O_7N_2 \cdot 3H_2O$  requires C = 63·35; H = 6·71 per cent.

*Brucine Benzoylpyruvate*,  $C_{10}H_8O_4C_{23}H_{26}O_4N_2 \cdot 2\frac{1}{2}H_2O$ . — Hard, colourless tablets, losing water at  $100^\circ$ , melting and decomposing at  $174^\circ$ :

0·1126 gave 0·2587  $CO_2$  and 0·0678  $H_2O$ . C = 62·66; H = 6·69.  
 $C_{33}H_{34}O_5N_2 \cdot 2\frac{1}{2}H_2O$  requires C = 62·76; H = 6·18 per cent.

Some of the amine salts employed in this work could not be obtained crystalline, or, at all events, sufficiently non-deliquescent for characterisation. Others, however, were definitely crystalline, and can be reported upon:

*Di-n-butylamine Camphorate*,  $C_{10}H_{16}O_4(C_4H_9NH_2)_2$ . — Delicate, white needles, melting at  $150-152^\circ$ :

0·1130 gave 0·2608  $CO_2$  and 0·1111  $H_2O$ . C = 63·17; H = 10·91.  
 $C_{15}H_{38}O_4N_2$  requires C = 62·94; H = 10·98 per cent.

*n-Butylamine Camphor- $\pi$ -sulphonate*,

$C_{10}H_{15}O \cdot SO_3H \cdot C_4H_9NH_2 \cdot 1H_2O$ . — Wax-like, shining crystals, melting at  $125^\circ$ :

0·1204 gave 0·2342  $CO_2$  and 0·1000  $H_2O$ . C = 53·06; H = 9·25.  
 $C_{14}H_{27}O_4NS \cdot 1H_2O$  requires C = 53·31; H = 9·22 per cent.

*Di-n-butylamine Tartrate*,  $C_6H_6O_6(C_4H_9NH_2)_2$ . — Cream, deliquescent prisms, melting at  $70-75^\circ$ .

*Dianiline Camphorate*,  $(C_6H_7N)_2C_{10}H_{16}O_4 \cdot 1\frac{1}{2}H_2O$ . — White, amorphous powder, softening at  $255-260^\circ$ :

0·1436 gave 0·3534  $CO_2$  and 0·0906  $H_2O$ . C = 67·11; H = 7·11.  
 $C_{22}H_{30}O_4N_2 \cdot \frac{1}{2}H_2O$  requires C = 66·83; H = 7·85 per cent.

*Diquinoline Camphorate*,  $(C_9H_7N)_2C_{10}H_{16}O_4 \cdot 2H_2O$ . — Deliquescent crystalline mass, melting at  $75-80^\circ$ :

0·1226 gave 0·3046  $CO_2$  and 0·0766  $H_2O$ . C = 67·76; H = 6·94.  
 $C_{25}H_{25}O_4N_2 \cdot 2H_2O$  requires C = 68·01; H = 6·88 per cent.

*Di- $\alpha$ -naphthylamine Camphorate*,  $(C_{10}H_9N)_2C_{10}H_{16}O_4 \cdot 2\frac{1}{2}H_2O$ . — Small needles, turning reddish-purple in the air, and melting at  $183^\circ$ :

0·1180 gave 0·2938  $CO_2$  and 0·0827  $H_2O$ . C = 67·90; H = 7·79.  
 $C_{30}H_{34}O_4N_2 \cdot 2\frac{1}{2}H_2O$  requires C = 67·79; H = 7·35 per cent.

*$\alpha$ -Naphthylamine Camphor- $\pi$ -sulphonate*,  $C_{10}H_9N \cdot C_{10}H_{15}O_4S$ . — Small, colourless flakes, turning blue-violet in the air, and melting at  $194-196^\circ$ :

0·1154 gave 0·2727 CO<sub>2</sub> and 0·0658 H<sub>2</sub>O. C = 64·45; H = 6·34.

C<sub>20</sub>H<sub>22</sub>O<sub>4</sub>NS requires C = 64·00; H = 6·37 per cent.

*α-Tetrahydro-α-naphthylamine Camphor-π-sulphonate,*  
C<sub>10</sub>H<sub>13</sub>N,C<sub>10</sub>H<sub>16</sub>O<sub>4</sub>S,4½H<sub>2</sub>O.

Glistening, colourless crystals, turning dark blue in the air, and melting somewhat indefinitely at 128—132°:

0·1053 gave 0·2016 CO<sub>2</sub> and 0·0854 H<sub>2</sub>O. C = 52·22; H = 8·49.

C<sub>20</sub>H<sub>22</sub>O<sub>4</sub>NS,4½H<sub>2</sub>O requires C = 52·17; H = 8·26 per cent.

*β-Naphthylamine Camphor-π-sulphonate*, C<sub>10</sub>H<sub>9</sub>N,C<sub>10</sub>H<sub>16</sub>O<sub>4</sub>S.—A cream-coloured, micro-crystalline powder, melting indefinitely at 118—121°:

0·1304 gave 0·2620 CO<sub>2</sub> and 0·0707 H<sub>2</sub>O. C = 54·80; H = 6·03.

C<sub>20</sub>H<sub>22</sub>O<sub>4</sub>NS,3½H<sub>2</sub>O requires C = 54·80; H = 5·84 per cent.

*Dianiline Tartrate*, (C<sub>6</sub>H<sub>7</sub>N)<sub>2</sub>.C<sub>4</sub>H<sub>6</sub>O<sub>6</sub>.—A soft, crystalline powder, turning pink in the air, but colourless again on heating; melts and decomposes at 184—185°:

0·1128 gave 0·2028 CO<sub>2</sub> and 0·0660 H<sub>2</sub>O. C = 49·05; H = 6·50.

0·0631 lost 0·0086 at 100°. H<sub>2</sub>O = 13·63.

C<sub>16</sub>H<sub>20</sub>O<sub>6</sub>N<sub>2</sub>.3H<sub>2</sub>O requires C = 49·22; H = 6·67;  
H<sub>2</sub>O = 13·85 per cent.

*Dipyridine Tartrate*, (C<sub>5</sub>H<sub>5</sub>N)<sub>2</sub>.C<sub>4</sub>H<sub>6</sub>O<sub>6</sub>.—Crisp, colourless flakes, melting at 158°:

0·1152 gave 0·2112 CO<sub>2</sub> and 0·0582 H<sub>2</sub>O. C = 49·99; H = 5·39.

C<sub>14</sub>H<sub>16</sub>O<sub>6</sub>N<sub>2</sub>.1½H<sub>2</sub>O requires C = 50·16; H = 5·67 per cent.

*Diquinoline Tartrate*, (C<sub>9</sub>H<sub>12</sub>N)<sub>2</sub>.C<sub>4</sub>H<sub>6</sub>O<sub>6</sub>.—A brick coloured, crystalline powder, melting at 131°:

0·1093 gave 0·2142 CO<sub>2</sub> and 0·0551 H<sub>2</sub>O. C = 53·44; H = 5·60.

C<sub>22</sub>H<sub>20</sub>O<sub>6</sub>N<sub>2</sub>.5H<sub>2</sub>O requires C = 52·99; H = 6·03 per cent.

*Bis-tetrahydroquinoline Tartrate*, (C<sub>9</sub>H<sub>11</sub>N)<sub>2</sub>.C<sub>4</sub>H<sub>6</sub>O<sub>6</sub>.—Crisp, cream-coloured flakes, turning green in air, and melting and decomposing at 118—120°.

*Dibenzylamine camphorate*, (C<sub>7</sub>H<sub>7</sub>·NII<sub>2</sub>)<sub>2</sub>.C<sub>10</sub>H<sub>16</sub>O<sub>4</sub>.½H<sub>2</sub>O, forms crisp, colourless crystals, melting at 188—189°:

0·1162 gave 0·2907 CO<sub>2</sub> and 0·0983 H<sub>2</sub>O. C = 68·21; H = 8·05.

C<sub>24</sub>H<sub>30</sub>O<sub>4</sub>N<sub>2</sub>.½H<sub>2</sub>O requires C = 68·10; H = 8·25 per cent.

*Benzylamine camphor-π-sulphonate* crystallised in slightly pink scales, darkening, without melting, at 230°.

*Dibenzylamine tartrate*, (C<sub>7</sub>H<sub>7</sub>·NH<sub>2</sub>)<sub>2</sub>.C<sub>4</sub>H<sub>6</sub>O<sub>6</sub>, consists of small, colourless needles, melting at 112°:

0·1100 gave 0·2263 CO<sub>2</sub> and 0·0678 H<sub>2</sub>O. C = 56·10; H = 6·85.

C<sub>18</sub>H<sub>24</sub>O<sub>6</sub>N<sub>2</sub> requires C = 56·54; H = 6·81 per cent.

*Menthyl Esters of Corresponding Aromatic Carboxylic and Sulphonic Acids.*

The carboxylic esters have already been described by Tschugaeff (*loc. cit.*); the samples of these compounds prepared by the author possessed melting points in agreement with Tschugaeff's data.

The sulphonate esters were prepared from the respective acid chlorides and menthol in the cold in the presence of pyridine, as recommended by Patterson and Frew (Trans., 1906, **80**, 332), who have described the benzene- and  $\beta$ -naphthalene-sulphonates of menthol. These esters are excellently adapted for polarimetric work, since they crystallise especially well, and are thus very easily and certainly purified.

*Menthyl p-Tolylsulphonate*,  $C_7H_7 \cdot SO_3 \cdot C_{10}H_{19}$ —Long, hard, stout, colourless needles, sparingly soluble in cold alcohol, and melting at  $97^\circ$ :

0·1418 gave 0·3424  $CO_2$  and 0·1105  $H_2O$ .  $C=65\cdot80$ ;  $H=8\cdot66$ .

0·1292 „ 0·0950  $BaSO_4$ .  $S=10\cdot09$ .

$C_{17}H_{20}O_3S$  requires  $C=65\cdot80$ ;  $H=8\cdot39$ ;  $S=10\cdot32$  per cent.

*Acyl Derivatives of Cinchonine and Cinchonidine.*

The *acetyl* compounds,  $CH_3 \cdot CO \cdot C_{19}H_{21}ON_2$ , were prepared by heating the alkaloids on the water-bath with excess of acetic anhydride for two hours. After cooling, the reaction mixture was poured into water and rendered alkaline with dilute sodium hydroxide. The products were then isolated by extraction with ether, and purified from unchanged base by solution in a large amount of boiling light petroleum, which was finally removed under diminished pressure at the ordinary temperature, leaving the compounds in the form of cream-coloured, amorphous powders:

*Acetylcinchonine* melted at  $51-53^\circ$ :

0·1138 gave 0·3118  $CO_2$  and 0·0716  $H_2O$ .  $C=74\cdot73$ ;  $H=6\cdot99$ .

$C_{21}H_{24}ON_2$  requires  $C=75\cdot01$ ;  $H=7\cdot14$  per cent.

*Acetylcinchonidine* melted at  $47-49^\circ$ :

0·1602 gave 0·4400  $CO_2$  and 0·0992  $H_2O$ .  $C=74\cdot88$ ;  $H=6\cdot90$ .

The benzoyl derivatives,  $C_6H_5 \cdot CO \cdot C_{19}H_{21}ON_2$ , resulted when 3 parts of the alkaloid and 5 parts of benzoyl chloride were boiled together in benzene solution for two hours. The product appeared as an oily hydrochloride, from which the benzene was removed by decantation and repeated washing with ether. The salt was then dissolved in cold water, and excess of ammonia added. The liberated base, after being filtered and dried, was usually rendered pure by one or two crystallisations from ether.

The *benzenesulphonyl* compounds,  $C_6H_5\cdot SO_2\cdot C_{19}H_{21}ON_2$ , were obtained in a precisely similar manner from equal weights of enzenesulphonyl chloride and cinchonine or cinchonidine.

*Benzoylcinchonine* crystallises in hard nodules from light petroleum or ether, but is too soluble in benzene or alcohol to crystallise well therefrom at the usual temperature. It melts somewhat indefinitely at 104–105°:

0·1574 gave 0·4510 CO<sub>2</sub> and 0·0982 H<sub>2</sub>O. C=78·14; H=6·93.

$C_{20}H_{20}O_3N_2$  requires C=78·39; H=6·54 per cent.

*Benzoylcinchonidine* separates from ether in small, hard needles, soluble in alcohol, insoluble in light petroleum, melting to a clear liquid at 183°:

0·1040 gave 0·2992 CO<sub>2</sub> and 0·0621 H<sub>2</sub>O. C=78·47; H=6·64.

*Benzenesulphonylcinchonine* crystallises from ether, but is almost insoluble in benzene:

0·1223 gave 0·3089 CO<sub>2</sub> and 0·0669 H<sub>2</sub>O. C=68·88; H=6·08.

$C_{25}H_{26}O_3N_2S$  requires C=69·11; H=5·99 per cent.

*Benzenesulphonylcinchonidine* may be obtained from a boiling benzene solution as small needles, melting at 166°:

0·1924 gave 0·4896 CO<sub>2</sub> and 0·1080 H<sub>2</sub>O. C=69·37; H=6·24.

The author takes this opportunity to acknowledge the assistance of a grant from the Research Fund of the Chemical Society in connexion with these investigations.

THE ORGANIC CHEMISTRY LABORATORY,  
UNIVERSITY COLLEGE, LONDON.

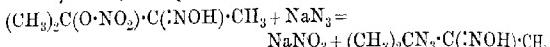
### XXVIII.—*The Triazo-group. Part XVI. Interaction of Nitrosates and Sodium Azide.*

By MARTIN ONSLOW FORSTER AND FREDERIK MARINUS VAN  
GELDEREN.

THE aliphatic azoimides which have been studied hitherto are derived from the corresponding halogen derivatives by double decomposition with sodium azide, a method of production which renders the azoimide nucleus comparable with the typical groups of the aliphatic nitriles, nitro-compounds, and carbimides. The fact that nitrosates, such as those of amyline and the terpenes, are capable of exchanging the nitroxyl group for NHX when treated with amines, giving rise to nitrolamines, led us to anticipate the

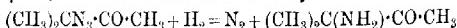
possibility of converting them into "nitrosoazides" by the action of sodium azide.

Our first experiments have been carried out with the nitrosate of *isoamylene* or trimethylethylene, originally prepared by Guthrie (*Annalen*, 1860, **116**, 248), and later by Wallach (*Annalen*, 1882, **245**, 243), who showed that potassium cyanide in aqueous alcohol transforms it into the nitrile of ketoximinodimethylacetic acid, an operation repeated by J. Schmidt (*Ber.*, 1902, **35**, 3726). On warming a suspension of the freshly prepared nitrosate in an alcoholic-aqueous solution of sodium azide, we found that the nitrosate is readily converted into the corresponding triazo-compound, "trimethylethylene nitrosoazide," or  $\beta$ -triazo- $\beta$ -methylbutan- $\gamma$ -oxime, with production of sodium nitrate,



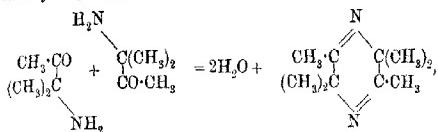
The triazo-oxime obtained in this way, unlike the material from which it is produced, is unimolecular, and is readily hydrolysed to the corresponding triazoketone,  $(\text{CH}_3)_2\text{CN}_3\cdot\text{CO}\cdot\text{CH}_3$ , which differs from earlier members of this class in the condition of the azoimide nucleus, since this is attached to a tertiary carbon atom. Comparison with triazocamphor (*Trans.*, 1905, **87**, 826), triazooacetone (*Trans.*, 1908, **93**, 81), and the triazo-derivatives of methyl ethyl ketone (*loc. cit.*, p. 673) shows that whilst these compounds, in which the triazotised carbon atom is either primary or secondary, lose approximately two-thirds the azidic nitrogen when treated with alcoholic sodium ethoxide, this agent acts quite differently on  $\beta$ -triazo- $\beta$ -methylbutan- $\gamma$ -one, which, although ultimately yielding nitrogen and ammonia, does so as the result of a profound alteration accompanied by the development of an intense, blood-red coloration; the oxime, however, is converted into a mixture of the unsaturated oximes,  $\text{CH}_2=\text{C}(\text{C}(\text{:NOH})\cdot\text{CH}_3)$ , unaccompanied by elemental nitrogen. Thus, the triazoketone establishes very clearly the principle suggested by the behaviour of triazomethylacetoacetic and triazooacetoacetic esters towards alkali (*Trans.*, 1910, **97**, 1360), namely, the dependence of the triazotised carbon atom upon hydrogen for the change first brought to light by the behaviour of camphorylazoinide towards alkali.

Early in the investigation it was recognised that the new triazoketone might prove to be a convenient source of  $\beta$ -amino- $\beta$ -methylbutan- $\gamma$ -one, which should arise from it by reduction:



The well-known work of Gabriel on aminoketones has shown that such substances readily undergo intermolecular condensation, yield-

ing pyrazine derivatives, but the comparative stability of  $\alpha$ -amino-camphor, coupled with the absence of hydrogen from the carbon atom associating the carbonyl and amino-groups in the above aminobutanone, led us to hope that it might resist the family tendency. Experiment showed, however, that although it is possible to produce the aminoketone in the form of a benzoyl derivative or salts, attempts to set it free from the latter by alkali led to hexamethylidihydropyrazine,



which forms a very characteristic hexahydrate, melting at 86–87°, and subliming with unusual readiness. It is not necessary for us to proceed with a description of this compound, however, because there has just appeared a communication by Gabriel (*Ber.*, 1911, **44**, 57), according to which the same substance is produced by combining phthaliminoisobutryl chloride with ethyl sodiummalonate and hydrolysing the product with hydriodic acid.

The interaction of trimethylene nitrosate and sodium azide suggested the possibility of converting terpenoid nitrosoates and nitrosoates into triazo-oximes which might be less easily obtained by other methods, and experiments in this direction, leading to dipentene nitrosoazide, will be described later. Moreover, since it is the nitroxyl group which lends itself to exchange, it should be possible to convert the nitric esters of aliphatic alcohols into the corresponding alkyl azoimides by interaction with sodium azide, and this we have found practicable in the case of *isoamyl* nitrate, which is converted, although with some difficulty, into *isoamyl* azoimide. Very recently it has been observed by Meldola and Kuntzen (this vol., p. 36) that an aromatic nitro-group in 2:3:5-trinitro-4-acetylaminophenol may be exchanged for an azoimide nucleus.

#### EXPERIMENTAL.

##### $\beta$ -Triazo- $\beta$ -methylbutan- $\gamma$ -oxime (*Trimethylene Nitrosoazide*), $(\text{CH}_2)_2\text{CN}_3\text{C}(\text{CH}_3)\text{NOH}$ .

Three hundred grams of amylene nitrosate, prepared from 430 c.c. (292 grams) of trimethylene, were divided into quantities of 16 grams; each portion was covered with 30 c.c. of alcohol, mixed with 4.5 grams of sodium azide in the minimum quantity of water, and heated gently until the appearance of bubbles indicated action,

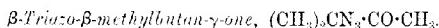
which was then allowed to proceed spontaneously. As a result of shaking and occasionally warming, the crystals slowly disappeared, forming a clear solution which at no stage was green or blue, and after an interval of twelve hours the accumulated liquid, containing crystals of sodium nitrate, was diluted largely with crushed ice, which precipitated lustrous, snow-white plates. The product was filtered and distilled in steam, yielding 94 grams of the solid oxime, a further quantity of which was obtainable from the mother liquor:

0·1617 gave 56·6 c.c. N<sub>2</sub> and 22° and 758 mm. N=39·40.

C<sub>6</sub>H<sub>10</sub>ON<sub>3</sub> requires N=39·44 per cent.

The triazo-oxime melts at 34—35°. It is freely soluble in organic media, and crystallises from ether in massive, transparent plates; hot water dissolves it sparingly. The cold substance has a faint odour of peppermint, but in steam the vapour has a pungent, overpowering odour, and exerts the worst physiological effects of the more volatile azoimides. Aqueous alkali neither dissolves it nor removes hydroxylamine, but the latter change is readily brought about by cold dilute sulphuric acid. With concentrated sulphuric acid the substance does not liberate gas until vigorously stirred, but with stannous chloride in hydrochloric acid effervescence quickly becomes brisk. A determination of molecular weight by depression of the freezing point gave the mean value 159 instead of 127. The benzoyl derivative is an oil.

*Reduction.*—On passing hydrogen sulphide into an alcoholic solution of the nitrosoazide rendered alkaline with ammonia, nitrogen was gradually liberated; when this change was complete, the liquid was evaporated, acidified with dilute sulphuric acid, filtered from sulphur, and shaken with benzoyl chloride in presence of sodium hydroxide. The solid product, after crystallisation from dilute methyl alcohol, melted at 142°, the temperature observed by Wallach for the dibenzoyl derivative of amylene nitrolamine (*Annalen*, 1891, **262**, 332).



Forty-five grams of the triazo-oxime were heated under reflux with 100 c.c. of 10 per cent. sulphuric acid on the water-bath during two to three hours, and the product extracted with ether; the residue from this was treated in the same way, and the operation repeated until the aqueous liquid failed to reduce cold Fehling's solution. The substance was then distilled under diminished pressure, 30 grams being obtained:

0·1440 gave 41·7 c.c. N<sub>2</sub> at 18° and 744 mm. N=33·25.

C<sub>6</sub>H<sub>9</sub>ON<sub>3</sub> requires N=33·07 per cent.

The triazoketone is a colourless liquid, having a pleasant, refreshing, peppermint-like perfume distinct from that of methyl ethyl ketone. It boils at 42°/14 mm., and decomposes without exploding at 170—180° under atmospheric pressure; the density is 1·057·182. The action with concentrated sulphuric acid and with stannous chloride is vigorous, but the substance is not affected by cold dilute alkali; if boiled with Fehling's solution, however, reduction takes place, accompanied by liberation of gas, and an odour of *isocyanide*.

The *semicarbazone*,  $(\text{CH}_3)_2\text{CN}_3\cdot\text{C}(\cdot\text{N}\cdot\text{NH}\cdot\text{CO}\cdot\text{NH}_2)\cdot\text{CH}_3$ , was prepared in the usual manner, and crystallised from benzene in rosettes of lustrous, colourless needles, melting at 127°:

0·1284 gave 51·0 c.c. N<sub>2</sub> at 21° and 754 mm. N = 45·75.

$\text{C}_6\text{H}_{12}\text{ON}_6$  requires N = 45·65 per cent.

The substance is readily soluble in cold chloroform and hot benzene, but boiling water or petroleum dissolves it sparingly, the former depositing six-sided prisms; it is indifferent towards alkali, and is rapidly hydrolysed by dilute hydrochloric acid.

The *thiosemicarbazone*,  $(\text{CH}_3)_2\text{CN}_3\cdot\text{C}(\cdot\text{N}\cdot\text{NH}\cdot\text{CS}\cdot\text{NH}_2)\cdot\text{CH}_3$ , arose on heating 2 grams of thiosemicarbazide in 50 per cent. alcohol with a slight excess of the triazoketone during two hours under reflux; on evaporating the solvent, there remained an oil which solidified when scratched. The product, weighing 3 grams, was dissolved in 7 c.c. of hot benzene, which deposited transparent, six-sided prisms, melting at 106—107°:

0·1386 gave 50·8 c.c. N<sub>2</sub> at 16° and 756 mm. N = 42·33.

$\text{C}_6\text{H}_{12}\text{SN}_6$  requires N = 42·00 per cent.

It is freely soluble in cold chloroform, but dissolves sparingly in hot petroleum; boiling water dissolves it more readily than the semicarbazone, and deposits long, lustrous needles as it cools. The thiosemicarbazone is quickly hydrolysed by cold dilute hydrochloric acid.

#### *Reduction of the Triazoketone.*

Numerous attempts were made to reduce  $\beta$ -triazo- $\beta$ -methylbutanone, with the object of studying the corresponding aminoketone, but, as already stated, we have been anticipated in this branch of the investigation by Gabriel (*loc. cit.*). Aluminium amalgam in ether, stannous chloride in hydrochloric acid, alcoholic ammonium sulphide, and zinc dust in acetic acid, all led to the characteristic hexahydrate of hexamethyldihydropyrazine, which is conveniently isolated in the form of the picrate. Of these processes the last-named was the most suitable, 2 grams of the triazoketone being dissolved in 20 c.c. of 50 per cent. acetic acid, and treated with

2 grams of zinc dust, added in very small quantities while the liquid was cooled; each addition of metal produced general effervescence throughout the liquid, which remained clear when the liberation of nitrogen was complete. Subsequent treatment consisted in adding excess of alkali, and passing steam through the liquid or extracting it with chloroform, which deposited the product in lustrous plates on spontaneous evaporation.

Our observations on the pyrazine derivative bear out in every respect those of Gabriel, and it is therefore superfluous to give a detailed description of the substance. The hexahydrate, which melts at 86—87° (Gabriel gives 88—89°), has a pronounced menthol-like odour, and sublimes freely in brilliant, transparent, quadratic prisms; after two or three days in the desiccator, the powdered substance was found to have changed into lustrous crystals of different geometrical form, melting incompletely at 50—52°. The picrate, on account of its sparing solubility in cold alcohol, is useful in recognising small quantities of the base: 2 grams, dissolved in 225 c.c. of boiling alcohol, separated in long lustrous, sulphur-yellow prisms, melting at 230° after becoming deep red:

0·1206 gave 18·9 c.c. N<sub>2</sub> at 17·5° and 740·5 mm. N=17·93.

C<sub>10</sub>H<sub>18</sub>N<sub>2</sub>C<sub>6</sub>H<sub>3</sub>O<sub>7</sub>N<sub>3</sub> requires N=17·72 per cent.

The platinichloride is insoluble in water, alcohol, acetone, and ethyl acetate, but was recrystallised from hot alcohol containing hydrochloric acid, which deposited small, transparent, pale red prisms, remaining solid at 310° (Pt=33·73; C<sub>10</sub>H<sub>20</sub>N<sub>2</sub>Cl<sub>6</sub>Pt requires Pt=33·86 per cent.).

With the object of preparing the aminoketone, the triazoketone was reduced with stannous chloride in hydrochloric acid, hydrogen sulphide being used to precipitate the tin; on adding alkali to the filtrate, and shaking with benzoyl chloride, the product melted at 125°, the temperature recorded by Gabriel.

ROYAL COLLEGE OF SCIENCE, LONDON,  
SOUTH KENSINGTON, S.W.

#### XXIX.—*The Triazo-group. Part XVII. Nitrosocides of Pinene and Terpineol.*

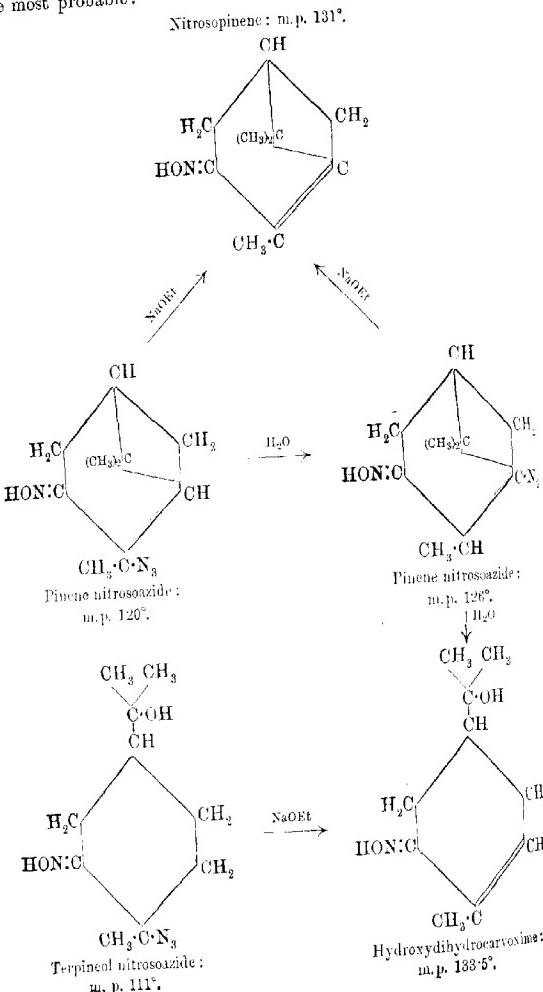
By MARTIN ONSLOW FORSTER and SIDNEY HERBERT NEWMAN.

DURING the thirty-five years which have elapsed since pinene nitrosochloride was characterised by Tilden, the substance itself, and the reaction upon which it is based, have continued to furnish data of interest and importance to the chemistry of the terpene

series. Early in the history of the nitrosochlorides, it was found that whilst the action of sodium ethoxide withdraws the elements of hydrogen chloride, treatment with a primary aliphatic amine involves an exchange of chlorine for the substituted ammonia residue, the products being called nitrolamines. Variations of this reaction have been described by Tilden and Burrows (*Trans.*, 1905, **87**, 341), Tilden and Leach (*Trans.*, 1904, **85**, 931), Leach (*Trans.*, 1907, **91**, 1), and Cusmano (*Gazzetta*, 1910, **40**, ii, 122), as the results of which pinene nitrosocyanide, the limonene nitroso-cyanides, pinene nitrolamine, and pinene hydroxylamineoxime, respectively, have been brought to light. The general applicability of this reaction suggested the possibility of introducing the triazo-group into the pinene nucleus by the action of sodium azide on the nitrosochloride, and we find that this change may be brought about very easily, the yield of nitrosoazide leaving little to be desired.

Pinene nitrosoazide is a unimolecular substance, melting at  $120^{\circ}$ , dissolving readily in organic media, and distilling slowly in steam. Alcoholic sodium ethoxide quickly removes the elements of hydrazoic acid, forming nitrosopinene, but the analogy to the nitrosochloride does not extend to the action of piperidine, for this base also produces nitrosopinene instead of the nitroso-piperidide, behaving, in fact, like diethylamine with the nitrosochloride. This indication of the presence of an *isonitroso*-group is confirmed by the production of an acetyl derivative (m. p.  $64^{\circ}$ ), but on attempting to convert the nitrosoazide into the triazoketone, as prescribed by Wallach (*Z. Naturf.*, 1906, **346**, 220) for the isolation of carvopinone from nitrosopinene, namely, hydrolysis with aqueous oxalic acid, it was found that hot water alone gives rise to an isomeric pinene nitroso-azide, melting at  $126^{\circ}$ , and yielding an acetyl derivative which melts at  $71^{\circ}$ . Two possibilities present themselves as an explanation of this change, either inversion of the carbon atom which carries the methyl and triazo-groups, or transference of the latter to a neighbouring atom, similar to the rearrangement which takes place when hydrogen chloride converts pinene into bornyl chloride. We believe that the latter alternative underlies the transformation in question. Although it is true that sodium ethoxide withdraws hydrazoic acid from the isomeric pinene nitrosoazide (m. p.  $126^{\circ}$ ), thereby producing nitrosopinene, the following formulæ made it clear that the latter might arise from an isomeride differing in structure from the original pinene nitrosoazide (m. p.  $120^{\circ}$ ). As, moreover, the action of hot water on the isomeride involves disruption of the tetramethylene ring, and leads to the oxime of hydroxydihydrocarvone with elimination of hydrazoic acid, it is natural to conclude that

it is one of the carbon atoms involved in this disruption which carries the azoimide nucleus; interchange of the latter with a methyl group being precluded, the representation we suggest seems the most probable:



The terpineol nitrosoazide represented above was prepared from inactive terpineol, melting at 35°, by converting it into the nitrosochloride, and acting on this with alcoholic aqueous sodium azide. Thus the hydroxydihydrocarboxime obtained from it by the action of sodium ethoxide is inactive also, and is identical with the specimen produced from the isomeric pinene nitrosoazide (*m. p.* 126°).

Progress has been made in the extension of this reaction to other nitrosochlorides, including those of limonene, and the results will be described later.

#### EXPERIMENTAL.

##### *Pinene Nitrosoazide, C<sub>10</sub>H<sub>14</sub>(NOH)·N<sub>2</sub>.*

Fifty grams of freshly prepared pinene nitrosochloride were suspended in 250 c.c. of 84 per cent alcohol containing 24 grams of sodium azide, and gently warmed; at the first sign of action, the flask was withdrawn from the steam-bath, and allowed to remain at about 40° during one hour. This treatment was repeated throughout the day, when it was found that the nitrosochloride had passed into solution, leaving a suspension of sodium chloride; the liquid was then diluted with water until crystallisation began. At no time was a blue or green colour noticed, and an occasional test for free hydrazoic acid gave only the faintest indication of that substance. The filtered product, which weighed 40 grams, was recrystallised from hot alcohol, then from a mixture of benzene and petroleum, and finally from benzene alone, 4 grams requiring about 15 c.c. of the hot solvent, which deposited brilliant, colourless, transparent prisms, melting to a colourless liquid at 120°:

0.2122 gave 0.4474 CO<sub>2</sub> and 0.1490 H<sub>2</sub>O. C = 57.50; H = 7.87.

0.0950 .. 22.0 c.c. N<sub>2</sub> at 18° and 767 mm. N = 27.13.

C<sub>10</sub>H<sub>14</sub>ON<sub>4</sub> requires C = 57.63; H = 7.74; N = 26.92 per cent.

The substance is freely soluble in cold ethyl acetate, chloroform, acetone, and hot benzene or alcohol, less readily in boiling petroleum. It is insoluble in 15 per cent. potassium hydroxide, and the solution in concentrated sulphuric acid effervesces only slowly on being stirred vigorously; with stannous chloride in hydrochloric acid, however, liberation of nitrogen takes place more actively. In steam the nitrosoazide is somewhat volatile, the vapour having a terpenoid and pungent odour, producing the disagreeable throbbing effect in the head which is so characteristic of the aliphatic azoimides. A determination of molecular weight by depression of the freezing point of benzene gave the mean value 227, C<sub>10</sub>H<sub>14</sub>ON<sub>4</sub> requiring 208.

*Conversion into Nitrospinene.*—The nitrosoazide was heated under reflux with alcohol in which one atomic proportion of sodium

had been dissolved, precipitation of sodium azide taking place very rapidly. After three hours the liquid was poured into water, which precipitated nitrospinene, identified with a specimen prepared from the nitrosochloride. The same substance, melting at 131°, was obtained by the action of piperidine in hot alcohol, this <sup>base</sup> failing to yield the nitrolpiperidide, which melts at 118—119°.

*The Acetyl Derivative.*—On heating pinene nitrosoazide with acetic anhydride during a few hours on the steam-bath, water precipitated a material which was recrystallised twice by diluting a solution in warm acetic acid:

0·1212 gave 23·2 c.c. N<sub>2</sub> at 20° and 774 mm. N=22·23.

C<sub>12</sub>H<sub>14</sub>O<sub>2</sub>N<sub>4</sub> requires N=22·41 per cent.

The substance is very freely soluble in organic media over petroleum, from which it separates in aggregates of tough, transparent, rectangular prisms, melting at 64°.

*The Isomeric Pinene Nitrosoazide* (m. p. 126°).

On subjecting a considerable quantity of the nitrosoazide (m. p. 120°) to steam distillation, it was noticed that the solid distillate even after recrystallisation, melted very indefinitely at 80—100°, whilst the residual liquid deposited lustrous, colourless needles melting at 133·5°, and no longer containing the triazo-group. Accordingly, 10 grams were heated under reflux during six hours on the steam-bath with about 100 c.c. of water and sufficient alcohol to ensure the return of the volatile nitrosoazide to the flask; a current of steam then carried over 3·5 grams of a colourless solid accompanied by a considerable proportion of hydrazoic acid, whilst the hot aqueous residue yielded about 3 grams of the substance melting at 133·5°. The distillate was recrystallised three times from hot petroleum, in which it is more readily soluble than the original nitrosoazide, forming lustrous, transparent, six-sided prisms melting at 126°:

0·1818 gave 0·3838 CO<sub>2</sub> and 0·1284 H<sub>2</sub>O. C=57·57; H=7·90.

0·1361 .. 31·3 c.c. N<sub>2</sub> at 17° and 764 mm. N=26·84.

C<sub>12</sub>H<sub>14</sub>ON<sub>4</sub> requires C=57·63; H: 7·74; N=26·92 per cent.

Thus the product appears to be isomeric with the original material, the melting point of which was depressed to about 100° by admixture. The presence of the triazo-group was revealed by effervescence with concentrated sulphuric acid and a hydrochloric acid solution of stannous chloride. The cold substance has a distinct, terpenoid colour, which becomes very pronounced in steam. A determination of molecular weight by depression of the freezing point of benzene gave the mean value 224, C<sub>10</sub>H<sub>16</sub>ON<sub>4</sub> requiring <sup>205</sup>.

*Action of Alcoholic Sodium Etheride.*—Two grams were heated

under reflux with 15 c.c. of alcohol, in which 0·3 gram of sodium had been dissolved, and having been poured into water after two hours, rendered faintly acid with acetic acid. The precipitate was crystallised first from alcohol, then from petroleum, when it melted at 131°, and did not depress the melting point of nitrosopinene when mixed with it.

*The Acetyl Derivative.* Three grams of the isomeride of pinene nitrosoazide (m. p. 126°) were heated with 10 c.c. of acetic anhydride during three hours on the steam-bath; the solid obtained on dilution was crystallised twice from dilute acetic acid, and finally from hot petroleum, which deposited aggregates of brittle, transparent plates, melting at 71°; a mixture of this product with the isomeric acetyl derivative (m. p. 64°) became liquid at about 50°:

0·1281 gave 24·0 c.c. N<sub>2</sub> at 18° and 781 mm. N = 22·20.

C<sub>13</sub>H<sub>18</sub>O<sub>3</sub>N<sub>4</sub> requires N = 22·41 per cent.

The substance is very freely soluble in organic media.

*Action of Hot Water.* Two grams of the nitrosoazide (m. p. 126°) were heated under reflux with water and a small quantity of alcohol during six hours, when a current of steam was passed through the liquid; 1·1 gram of unchanged material was carried over, along with hydrazoic acid, whilst the residual liquid deposited lustrous needles identical with the above-mentioned by-product melting at 133·5°. This was found on analysis to have the composition C<sub>10</sub>H<sub>17</sub>O<sub>2</sub>N:

0·1649 gave 0·3976 CO<sub>2</sub> and 0·1431 H<sub>2</sub>O. C = 65·77; H = 9·70.

0·2273 ... 15·4 c.c. N<sub>2</sub> at 17° and 759 mm. N = 7·85.

C<sub>10</sub>H<sub>17</sub>O<sub>2</sub>N requires C = 65·57; H = 9·37; N = 7·65 per cent.

We were thus led to suspect identity with the oxime of hydroxy-dihydrocarvone, stated by Wallach to melt at 133-134°, and on preparing the diacetyl derivative from our product, this melted at 107°, the temperature recorded by Wallach for that substance. The presence of the oximino group was further indicated by the action of hot dilute sulphuric acid, which eliminated hydroxylamine.

*The Benzoyl Derivative.*—By the action of benzoyl chloride in 10 per cent. sodium hydroxide, a monobenzoyl derivative was produced:

0·2194 gave 9·8 c.c. N<sub>2</sub> at 17° and 764 mm. N = 5·12.

C<sub>17</sub>H<sub>21</sub>O<sub>2</sub>N requires N = 4·88 per cent.

It melts at 83-84° after crystallisation from a mixture of benzene and petroleum.

*Terpineol Nitrosoazide*,  $C_{10}H_{16}(OH)(NOH) \cdot N_3$ .

Thirteen grams of nitrosochloride, prepared from inactive terpineol (m. p.  $35^\circ$ ), were suspended in 100 c.c. of 84 per cent. alcohol, and allowed to remain with 6 grams of sodium azide at about  $40^\circ$  until the suspended material consisted of sodium chloride. This occupied a few hours, and did not involve change of colour or liberation of hydrazoic acid. On pouring the product into water, terpineol nitrosoazide separated as an oil which solidified very slowly, the first crop weighing 5 grams; a further quantity separated from the mother liquor in the course of another week. The product was moistened with cold petroleum, drained on earthenware, and recrystallised twice from the minimum quantity of hot benzene, which deposited clusters of small, transparent, six-sided plates, melting at  $111^\circ$ :

0·1717 gave 0·3337 CO<sub>2</sub> and 0·1244 H<sub>2</sub>O. C=53·01; H=8·11.

0·0952 „, 20·2 c.c. N<sub>2</sub> at  $19^\circ$  and 779 mm. N=25·01.

$C_{10}H_{18}O_2N_4$  requires C=53·05; H=8·02; N=24·80 per cent.

The substance is freely soluble in organic media, excepting petroleum, which dissolves it sparingly on boiling; it is also somewhat soluble in cold water, crystallising slowly in long, six-sided prisms. The nitrosoazide is odourless, even in boiling water, but the azidic character is revealed by effervescence with concentrated sulphuric acid and a hydrochloric acid solution of stannous chloride. When heated with alcoholic sodium ethoxide, sodium azide is precipitated, and hydroxydihydrocarboxime is formed (m. p. 133·5°).

ROYAL COLLEGE OF SCIENCE, LONDON.  
SOUTH KENSINGTON, S.W.

XXX.—*New Derivatives of d-Glucosamine.*

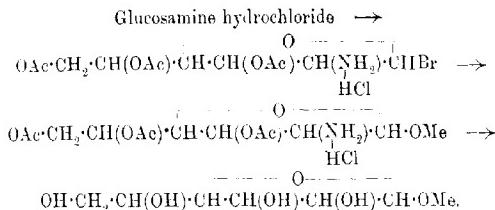
By JAMES COLQUHOUN IRVINE, DAVID McNICOLL, M.A., B.Sc. (Carnegie Scholar), and ALEXANDER HYND, M.A., B.Sc. (Carnegie Scholar).

THE action of acetyl bromide on reducing sugars, by means of which the latter are converted into aceto-halogen derivatives, has recently been extended considerably by Fischer and his pupils (*Ber.*, 1909, **42**, 2776; 1910, **43**, 2521). Owing to their convenient solubilities, the ready displacement of the halogen atom, and the ease with which the acetyl groups may be subsequently eliminated, these acetylated

mono-compounds are likely to prove of great service in sugar synthesis. In particular, the preparation by Fischer of non-reducing disaccharides by self-condensation of acetylated aldoses opens up a new field in the formation of sugar complexes.

Towards the close of 1908 a research was commenced in this laboratory on the constitution of glucosamine, and the paper published by one of us, "A Polarimetric Method of Identifying Chitin" (Trans., 1909, **95**, 564), contained some results which were obtained in the early part of the work. The action of acetyl bromide on glucosamine hydrochloride was subsequently undertaken with the object of preparing a bromotriacetylglucosamine from which a triacetyl methylglucosamine could be obtained. Presumably a glucoside of this nature would, owing to the absence of hydroxyl groups, react normally with nitrous acid, and thus be converted ultimately into methyl glucoside. Additional evidence of a peculiarly direct nature would thus be obtained as to the relationship between glucosamine and glucose.

The theoretical steps in the scheme of reactions is shown below:



The experimental difficulties encountered have delayed the completion of the research on the above lines, and, during the progress of the work, important papers have been published by Fischer on the application of acetyl bromide as a reagent in the sugar group. Owing to the similarity of the methods employed by us, we considered it advisable to submit our results to Professor Fischer so as to avoid duplication, and, in a private communication, he kindly informed us in advance of the details of his recent research on amino-sugars (*Ber.*, 1911, **44**, 132). The investigation in question includes the preparation of an aminomethylglucoside, which, in his opinion, does not appear to be a derivative of glucosamine, and as our work has now resulted in the formation of an aminoglucoside which is possibly identical with Fischer's, we have arranged to publish our results simultaneously and in a less complete form than otherwise would be desirable.

We find that glucosamine hydrochloride reacts with acetyl bromide to give bromotriacetylglucosamine hydrobromide (m. p.

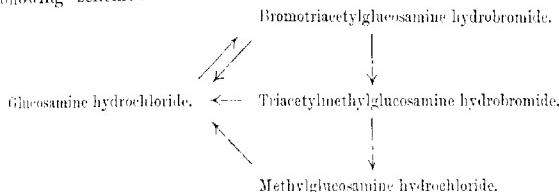
149–150°,  $[\alpha]_D + 148.4^\circ$ ). The salt-forming molecule of hydrogen chloride originally present is thus displaced by hydrogen bromide but otherwise the reaction is normal, and the primary amino-group is not affected by the reagent. The product displays the usual properties of an aceto-halogen sugar derivative. When dissolved in moist acetone, hydrogen bromide is formed, and, in the absence of a base, the acetyl groups are slowly eliminated, so that glucosamine hydrobromide is finally produced. The conversion into a "methyl glucoside" was effected by dissolving the bromo-compound in methyl alcohol containing one molecular proportion of pyridine, the product of the change being triacetyl methylglucosamine hydrobromide (m. p. 230–233°,  $[\alpha]_D + 20.26^\circ$ ). This compound behaved as a glucoside towards Fehling's solution, and contained one methoxy group. The action of nitrous acid on the substance confirmed the presence of the amino-group, but the acetyl groups were also eliminated during the reaction, and, so far, no definite derivative of glucose has been isolated from the products.

The hydrolysis of triacetyl methylglucosamine hydrobromide, when carried out with concentrated hydrochloric acid, resulted in the formation of glucosamine hydrochloride, but the hydrolysis may be controlled so that only the acetyl groups are removed, while the glucosidic methoxyl group remains unaltered. This was effected by boiling with barium hydroxide in aqueous solution and also by the prolonged action of a 0.75 per cent. methyl-alcoholic solution of hydrogen bromide in the cold. In either case, a non-acetylated aminomethylglucoside results, which, in the meantime, may be termed *methylglucosamine*. The compound reacts strongly basic and forms a well-defined hydrochloride (m. p. 185°), which gives  $[\alpha]_D - 19.5^\circ$  in aqueous solution. It has no action on Fehling's solution until after hydrolysis, and reacts as an amino-compound towards nitrous acid. The latter reaction has, so far, only been carried out on the small scale, but we intend to examine the products of the change with the object, if possible, of isolating methylglucoside.

The aminomethylglucoside recently prepared by Fischer from dibromotriacetylglucose (*b.c. cit.*) shows many similarities with that just described, but it is difficult in the meantime to say definitely if the compounds are isomeric or identical. It is important to arrive at a decision on this point, as, assuming the compounds to be identical, a direct synthesis of glucosamine from glucose is thus established by Fischer. A comparison of the two compounds is therefore included in the discussion which follows. In the course of the work, triacetylglucosamine hydrobromide and a dibarium derivative of glucosamine were isolated as by-products.

*Discussion of Results.**Constitution and Nomenclature of the Compounds Described.*

As, in addition to the correlation of glucosamine and glucose, the object of the present research is the synthesis of complexes containing the glucosamine residue, it is important that the constitution of the compounds involved should be established. Each substance has accordingly been hydrolysed, and the products have been identified. This was considered necessary in view of the fact that, in the decomposition of bromotriacetylglucosamine, pyridine was used to remove hydrogen bromide, and, in the subsequent preparation of methylglucosamine, silver carbonate was employed for the same purpose. Neither reagent seems, however, to have occasioned intramolecular changes, as all the compounds described gave either glucosamine hydrobromide or hydrochloride on complete hydrolysis. This definite relationship to glucosamine is therefore embodied in the nomenclature used, and is shown in the following scheme:



Each of the new derivatives should, like the parent substance, exist in  $\alpha$ - and  $\beta$ -modifications, and, in the case of bromotriacetylglucosamine, the two forms should be spontaneously interconvertible. This was confirmed by examination of solutions in anhydrous non-hydroxy solvents, optical changes then resulting which were not due to decomposition, and which must therefore be regarded as normal mutarotation. The change was difficult to detect, as minute traces of moisture decompose the bromo-compound and give rise to apparent mutarotation, but the following result shows that the compound is precipitated from solution in a labile form.

*Solvent: Pure dry acetone.  $c = 5.01$ .*

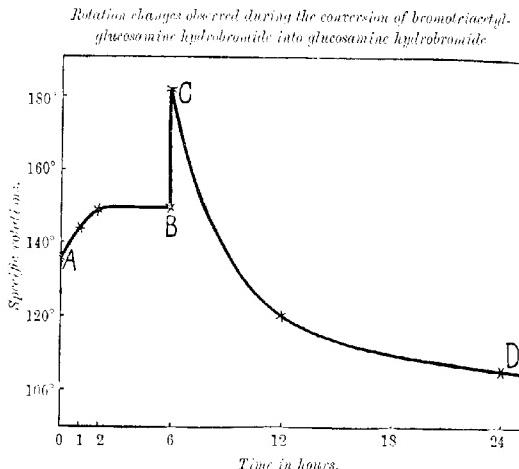
Time from first reading.	[ $\alpha$ ] $D^25$ .
0 minutes .....	+135.9°
60 " .....	143.9°
90 " .....	148.4 (approximately constant)

The equilibrium solution was then diluted to half the concentration with acetone containing 2 per cent. of water. The

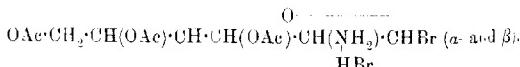
specific rotation at once increased to  $+181.6^\circ$ , and then diminished gradually, as shown below:

Specific rotation before addition of aqueous acetone.....	$+148.1^\circ$
" " after	$181.6^\circ$
" " 12 hours later.....	$120.9^\circ$
" " 36 " "	$94.3^\circ$
" " 240 " "	$113.0^\circ$

A crystalline substance gradually separated, from the third day onwards, until finally nothing remained in solution. This product, when recrystallised from methyl alcohol, was shown to be glucosamine hydrobromide. The interpretation of the optical changes is simplified by plotting the values in a curve:

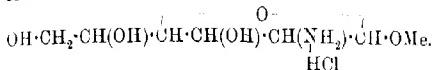


Normal mutarotation in the pure solvent is represented by *AB*, the immediate formation of triacetylglucosamine by the sharp rise *BC*, whilst *CD* represents the gradual removal of the acetyl groups and the precipitation of the product from solution. From these considerations, we regard the bromo-compound as possessing the structure:



Considering the method employed in the preparation of a methyl-glucoside from the above compound, the product should be the  $\beta$ -form. This is supported by the low value of the specific rotation.

and by the fact that different preparations gave uniformly the same result. On the other hand, inspection of the experimental details will show that our preparation of methylglucosamine probably consists of a mixture of the  $\alpha$ - and  $\beta$ -forms:



This complicates comparison with Fischer's aminomethylglucoside hydrochloride. The solubilities and crystalline forms of the two substances are similar, but whilst Fischer's compound gives  $[\alpha]_D -25.1^\circ$  and decomposes at  $210^\circ$ , we find that methylglucosamine hydrochloride gives  $[\alpha]_D -19.5^\circ$ , and melts indefinitely at  $185-187^\circ$ . These differences might, however, be explained on the assumption that the two preparations are mixtures of  $\alpha$ - and  $\beta$ -forms in different proportions, the melting point in one case being lowered below the decomposition point. A more serious point of apparent distinction is the behaviour of the compounds towards hydrolytic agents. Fischer's aminoglucoside is hydrolysed by *N*-hydrogen chloride at  $100^\circ$  to give a product other than glucosamine hydrochloride. On the other hand, we find that methylglucosamine is only hydrolysed to a slight extent by similar treatment. Even after heating for two hours at  $100^\circ$  with 10 per cent. hydrochloric acid, only a slight rise of rotatory power in the dextro-sense was evident, and, as rotatory changes during the hydrolysis of glucosides are usually well marked, we conclude that the change is imperfect under the given conditions. It should be stated, however, that, during the action, the liquid acquired a very decided action on Fehling's solution, and the product, when isolated, no longer behaved definitely as a glucoside. The use of concentrated hydrochloric acid as the hydrolytic agent gave, however, a normal result, the specific rotation rapidly altering from  $-17^\circ$  to  $+52^\circ$ , and glucosamine hydrochloride was then isolated in nearly quantitative amount from the solution. It would thus appear that the glucosidic group in methylglucosamine is either remarkably stable, or that the hydrolysis of the compound is accompanied by the formation of intermediate complexes, which are only decomposed into glucosamine hydrochloride by concentrated acid. It is also conceivable that, if hydrolysed polarimetrically with concentrated acid, Fischer's compound may similarly give the glucosamine salt. This, as already pointed out, would be a highly desirable result.

## EXPERIMENTAL.

*Preparation of Glucosamine Hydrochloride.*

The starting material used was chitin, which was prepared from lobster shells in the usual way. The product was not precipitated and was therefore in the massive state. The conversion into the glucosamine salt by boiling with hydrochloric acid results in some decomposition, but we have succeeded in increasing the yield considerably by carrying out the hydrolysis according to the method described by one of us for polarimetric experiments (*loc. cit.*). As the economical preparation of glucosamine hydrochloride is important, we submit the details of one typical experiment.

Fifty grams of dry chitin were vigorously shaken in a wide-mouthed bottle with 1250 c.c. of concentrated hydrochloric acid for six hours. A clear, syrupy solution was thus obtained, and the hydrolysis was completed by heating at 50° for an additional period of six hours, the liquid being vigorously stirred during the process. The solution, which was only slightly brown, was then concentrated nearly to dryness at 50°/15 mm. Absolute alcohol (150 c.c.) was then added, and the crude glucosamine salt collected. The product, when recrystallised in the usual manner, amounted to 80 per cent. of the weight of chitin used, and no gummy by-products were formed. A quantity of 200 grams of the glucosamine salt, prepared by the above process, was used in the following experiments.

*Bromotriacetylglucosamine Hydrobromide.*

In the preparation and manipulation of this compound, all the materials used must be specially dried, and precautions taken to exclude moisture. As the action of acetyl bromide on glucosamine hydrochloride is vigorous, and the bromoaceto-derivative formed is decomposed by the reagent, the best conditions for the preparation of the compound were only ascertained after a large number of experiments had been made. The reaction must be carried out with small quantities of material, and, in order to avoid the necessity to weigh out the reagent, the best method is to use in each preparation the weight of glucosamine salt corresponding with the weight of acetyl bromide contained in a tared sealed bottle. The following are the details of one typical preparation. 8·4 Grams of glucosamine hydrochloride (1 mol.) were introduced into a boiling tube fitted with a reflux condenser and provided with a mechanical stirrer working in a mercury seal. Twenty-five grams (5 mols.) of acetyl bromide were then added, and the well-stirred mixture cautiously heated. Reaction usually commenced at 60°, and

hydrogen bromide was steadily evolved for thirty minutes, after which the mixture suddenly solidified. The tube, when cold, was broken in a mortar, the hard mass roughly powdered, and kept in a vacuum desiccator over soda-lime until free from hydrogen bromide. The yield of crude material thus obtained was almost the theoretical amount, and no unchanged glucosamine hydrochloride remained.

The use of a larger proportion (9 mols.) of acetyl bromide than that recommended above is inadvisable, as the product remains in solution, and no definite end-point to the reaction can be detected, as hydrogen bromide is continuously evolved owing to decomposition of the product. The use of the theoretical amount of the reagent is also inconvenient, as about 20 per cent. of the glucosamine salt escapes reaction. It was also impossible to carry out the reaction successfully in chloroform solution, as apparently triacetylglucosamine hydrobromide resulted.

The crude bromo-compound was dissolved in hot chloroform, filtered from traces of glucosamine salts, and the solution allowed to evaporate spontaneously until crystals formed on the side of the crystallising basin. After the addition of a small quantity of dry ether, the solution was vigorously stirred, and in a few minutes the purified compound suddenly separated. When pure, bromotriacetylglucosamine hydrobromide consists of colourless, delicate needles, softening at 144°, and melting and decomposing at 149-150°. The compound is readily soluble in water, methyl or ethyl alcohols, acetone or ethyl acetate, reacting with the hydroxy-solvents, but is insoluble in ether or hydrocarbons:

Found, C=32·05; H=4·47; Br=34·66; N=3·17.

$C_{12}H_{15}O_7NBr \cdot HBr$  requires C=32·08; H=4·28; Br=35·02; N=3·12 per cent.

Unless specially purified, the compound rapidly acquired a pink colour, but a pure specimen has now remained colourless for several months.

Permanent specific rotation in acetone ( $\nu = 5\cdot91$ ) .....	.....	+148·4°
" " " ethyl acetate ( $\nu = 1\cdot096$ ) .....	.....	+152·8

The above values gradually diminished after some time, owing to hydrolysis.

#### *Triacetyl/methylglucosamine Hydrobromide.*

A 5 per cent. solution of bromotriacetylglucosamine hydrobromide was prepared in absolute methyl alcohol containing 1 per cent. of anhydrous pyridine. Optical examination of the filtered liquid showed that the reaction was complete after six hours at

the laboratory temperature, and that the reaction is quantitative. The solvent was removed at 20°/15 mm., and the residue crystallised from methyl alcohol containing a small quantity of ether. A trace of moisture during all the operations must be carefully excluded, as otherwise the deliquescence of the pyridine salt results in the formation of syrupy products. A small quantity of glucosamine hydrobromide is also produced, and the yield of the pure glucoside isolated does not exceed 52 per cent. of the theoretical amount.

Found, C=38·94; H=5·83; Br=20·10; N=3·70; OMe=7·50.  
 $\text{C}_{12}\text{H}_{18}\text{O}_7\text{N}(\text{OMe})\text{HBr}$  requires C=38·99; H=5·55; Br=19·97;  
 N=3·50; OMe=7·74 per cent.

Triacetyl methylglucosamine hydrobromide crystallises in delicate prisms, melting and completely decomposing at 230—233°. The compound is readily soluble in water or alcohol, sparingly so in acetone, insoluble in ethyl acetate, chloroform, ether, or benzene. The aqueous solution reacts feebly acid to litmus, and behaves as a glucoside towards Fehling's solution. Ammonia is evolved when the compound is boiled with sodium hydroxide, the solution turning brown.

Solvent.	v.	Specific rotation.
Methyl alcohol.....	2·098	+20·26° (without mutarotation)
Water .....	1·240	20·56 " "

#### *Hydrolysis of Triacetyl methylglucosamine Hydrobromide.*

*Complete Hydrolysis by Hydrogen Chloride.*—A 5 per cent. solution in concentrated hydrochloric acid was kept for twelve hours at 20°. During this time the specific rotation diminished from +25·5° to -6°, owing to the removal of the acetyl groups. The solution was then heated in boiling water, polarimetric readings being taken at intervals. The rotation rapidly became dextro, and after forty minutes the value was  $[\alpha]_D^{20} +16^{\circ}$ . Thereafter the liquid suddenly turned brown, so that no further optical examination was possible. The solvent was removed at 30°/15 mm., the residue washed with alcohol, and recrystallised from water by the addition of alcohol. The product reduced Fehling's solution, gave the nitrous acid test, and was shown to be glucosamine hydrochloride by determination of the specific rotation and halogen content:

Found,  $[\alpha]_D^{20}$  in water +89·6° → 71·5°; Cl = 16·55 per cent.

Glucosamine hydrochloride requires  $[\alpha]_D^{20}$  → 72·5°.

Cl = 16·44 per cent.

*Partial Hydrolysis by Barium Hydroxide.*—3·3 Grams of triacetyl-methylglucosamine hydrobromide were dissolved in 100 c.c. of an aqueous solution of barium hydroxide containing 7·81 grams  $\text{Ba}(\text{OH})_2 \cdot 8\text{H}_2\text{O}$ , and the liquid was boiled under a condenser for

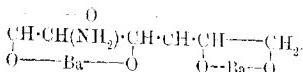
forty-five minutes. The equivalent amount of *N*-sulphuric acid was then added, and, after removing the barium sulphate, the solution was evaporated at 30°/15 mm. The solid residue was extracted in the first place with boiling ethyl alcohol, and afterwards with cold methyl alcohol. The former extract gave, on evaporation, a syrup which reduced Fehling's solution. This was dissolved in excess of methyl alcohol containing 0·25 per cent. of hydrogen chloride, and heated at 90° for twelve hours. The acid was removed by means of silver carbonate, and the filtrate, on evaporation in a vacuum, yielded a syrup which reacted as a strong base. On dissolving in cold concentrated hydrochloric acid and precipitating with excess of acetone, a crystalline precipitate was obtained. This proved to be the hydrochloride of methylglucosamine which is subsequently described.

The methyl-alcoholic extract described above, when decolorised and evaporated, yielded a semi-crystalline residue. After drying on porous porcelain and recrystallisation from methyl alcohol, the product was found to be free from halogen, but contained barium. Analysis of a specimen dried at 100° gave:

Found, C=14·14; H=1·93; Ba=61·41.

$C_6H_{10}O_5N\text{Ba}_2$  requires C=16·00; H=2·01; Ba=61·10 per cent.

Owing to the small quantity of material available for combustion, the analytical values are only approximate, but, taken in conjunction with the barium estimation, indicate that the compound possesses the structure:



As it is unlikely that the glucosidic methoxyl group would be removed by the alkali, the above product seems to have resulted from impurities present in the glucoside used. Similar compounds have been obtained by Fischer in the hydrolysis of acetylated sugars, and the general stability of these barium derivatives is remarkable.

*Partial Hydrolysis by Hydrogen Bromide.*—A 5 per cent. solution of the glucoside salt in water containing 2 per cent. of hydrogen bromide was heated for several hours at 50°. The optical change was very slight, indicating slow removal of the acetyl groups. At 90° the action was more rapid, the specific rotation diminishing in three hours from +19·5° to -6·5°. The acid was removed by means of silver carbonate, the free base isolated as already described, and converted into the hydrochloride. The same product was obtained free from action on Fehling's solution by dissolving triacetyl-methylglucosamine hydrobromide in methyl alcohol containing 0·75 per cent. of hydrogen bromide, and keeping the solution in the

dark until the rotation became constant. The optical change was complete in about twenty days, the product being converted into the hydrochloride as described above. The method of slow hydrolysis obviates the necessity to remove traces of reducing sugar by condensation with methyl alcohol.

*Action of Nitrous Acid.*—The reaction was carried out by shaking an alcoholic or aqueous solution of the hydrobromide with silver nitrite. In the former case the evolution of nitrogen was slow and the decomposition of the amino-group imperfect, but in aqueous solution the reaction appeared to proceed normally. The isolation of the product was carried out by the method adopted by Fiske but in each case it was found that the acetyl groups had been partly removed, and that the syrup obtained reduced Fehling's solution actively. Attempts to convert the mixed products into a glucoside or into a definite hexose have so far been unsuccessful but the properties of the syrup differ from those of chitosan, and the reaction is being repeated.

#### *Methylglucosamine Hydrochloride.*

This compound, when prepared by the methods already described, crystallises in needles melting and decomposing at 185–187°. Analysis of a specimen dried at 95° gave:

Found, C = 36·17; H = 7·17; Cl = 15·09; OMe = 12·57.  
 $C_6H_{12}O_4N(OMe) \cdot HCl$  requires C = 36·58; H = 7·02; Cl = 15·44;  
 OMe = 13·51 per cent.

*Methylglucosamine hydrochloride* is readily soluble in water and methyl alcohol, and behaves as a glucoside towards Fehling's solution. Nitrogen is evolved on the addition of nitrous acid, and ammonia is disengaged when the compound is boiled with sodium hydroxide, the liquid turning brown. The compound apparently exists in  $\alpha$ - and  $\beta$ -modifications, as different preparations showed a variation in melting point and specific rotation:

M. p. 187°. Solvent: methyl alcohol.	c = 2·581.	$[\alpha]_D^{20} = 16·7^\circ$ (no mutarotation)
„ 180° „ „ „	c = 2·150.	$[\alpha]_D^{20} = 13·95^\circ$ „ „
„ 180° „ water	c = 3·892.	$[\alpha]_D^{20} = 19·5^\circ$ „ „

As our preparation may not be a pure stereochemical form, the above values are liable to subsequent correction.

#### *Hydrolysis of Methylglucosamine Hydrochloride.*

*Complete Hydrolysis by Hydrogen Chloride.*—A 2·046 per cent. solution of the glucoside salt in concentrated hydrochloric acid was heated in boiling water for fifteen minutes. The specific rotation altered from  $-17^\circ$  to  $+52^\circ$ , and the liquid turned brown. The

hydrolysis was then complete, as glucosamine hydrochloride in similar concentration and similarly dissolved gives  $[\alpha]_D + 52^\circ$  (*loc. cit.*). The solvent was removed at  $30^\circ/15$  mm., and the crystalline residue of glucosamine hydrochloride purified as usual:

Found.  $[\alpha]_D^{25} + 94.4^\circ \rightarrow 71.7^\circ$ . Cl = 16.71 per cent.

Glucosamine hydrochloride requires  $[\alpha]_D^{25} \rightarrow 72.5^\circ$ .

Cl = 16.44 per cent.

*Action of Dilute Hydrochloric Acid.*—A 1.5 per cent. solution of methylglucosamine hydrochloride in water containing 5 per cent. of hydrochloric acid was heated for two hours at  $100^\circ$ . The optical change then observed was  $[\alpha]_D - 18.3^\circ \rightarrow -17.7^\circ$ . The concentration of acid was then increased to 10 per cent., and the solution heated for three hours in boiling water. During the treatment with even the more dilute acid, the solution acquired a decided action upon Fehling's solution, but with the higher concentration of acid the optical change was only  $[\alpha]_D - 17.7^\circ \rightarrow +7.3^\circ$ , and apparently only 25 per cent. of the glucoside was hydrolysed. The product, isolated as usual, resembled the original material, melted indefinitely at  $172^\circ$ , reduced Fehling's solution strongly, and gave  $[\alpha]_D - 5^\circ$  in methyl-alcoholic solution. Owing to lack of material, we were unable to confirm our idea that the reducing action was due to the presence of a small quantity of glucosamine hydrochloride. The ready solubility of the product in methyl alcohol is not against this assumption, as it is possible to obtain a 0.892 per cent. solution of glucosamine hydrochloride in methyl alcohol. It is thus evident that the method of purification employed, namely, solution in methyl alcohol and precipitation with ether, would only give a pure product when carried out on a scale sufficiently large to permit of fractional precipitation.

The research is being continued on the lines indicated in this communication.

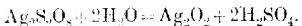
The authors take the opportunity of expressing their indebtedness to the Carnegie Trust for a grant in aid of the investigation, and of expressing their appreciation of the courtesy shown them by Professor Emil Fischer.

CHEMICAL RESEARCH LABORATORY,  
UNITED COLLEGE OF ST. SAVIATOR AND ST. LEONARD,  
UNIVERSITY OF ST. ANDREWS.

*XXXI.—The Interaction of Silver Nitrate and Potassium Persulphate and its Catalytic Effect in the Oxidation of Organic Substances,*

By PERCY CORLETT AUSTIN.

WHEN aqueous solutions of silver nitrate and potassium persulphate are mixed, a black precipitate is formed, of which no analysis has hitherto been published. This subject has already received attention by Marshall (*Proc. Roy. Soc. Edin.*, 1900, **23**, 163), and by Marshall and Inglis (*ibid.*, 1902, **24**, 88). The assumption was made that silver persulphate is first formed, and that this rapidly decomposes with water according to the equation:



At the suggestion of Professor Inglis, I have investigated this product, and have also studied the catalytic effect produced by adding a trace of silver nitrate to aqueous solutions of potassium persulphate in the presence of organic substances. A study of the results obtained by careful analysis indicates the correctness of the above assumption, the black precipitate consisting of a mixture of silver peroxide, silver persulphate, and water, in proportions which varied somewhat, according to the conditions under which it was prepared. The appended results were all obtained from the same specimen.

In the preparation of the precipitate for analysis, various proportions were tried, the best results being obtained by using about two molecules of potassium persulphate to one of silver nitrate. Owing to the sparing solubility of potassium persulphate in water, the solutions employed were necessarily very dilute. The dilution used was also sufficient to prevent the separation of silver sulphate, the presence of which was at one time suspected.

Ten grams of silver nitrate dissolved in 100 c.c. of distilled water were added to a solution of 30 grams of potassium persulphate in a litre of water, at the ordinary temperature, in a large separating funnel, the mixture being thoroughly shaken. The formation of the black precipitate, although not immediate, quickly followed. Owing to the difficulty of filtering such a solution, since the persulphate attacks filter-paper, it was kept for about an hour, by which time the bulk of the precipitate had settled and could be drawn off. It was immediately shaken with distilled water, washed three or four times by decantation, and finally filtered and washed again. It was then spread out on a watch-glass and dried in a vacuum desiccator over sulphuric acid. The drying was found to

so pure several days. The substance was indeed allowed to remain thus for some weeks, when it was transferred to a stoppered weighing bottle, and kept in a desiccator. Owing to its hygroscopic nature, it could not be weighed on an open watch-glass. The substance was then analysed.

Heating it in a crucible gave unsatisfactory results, since it decomposes explosively at about  $110^{\circ}$ , and although several trials were made by heating it in covered crucibles in the air-oven, there was always a loss by spitting. A qualitative examination of the residue, which was soluble in nitric acid, showed the presence of a sulphate. This might have been originally present as such or as persulphate. The residue was also tested for nitrate by dissolving in sulphuric acid and applying the ferrous sulphate test. No trace of nitrate could be found. Eventually determinations were made of silver by conversion into silver chloride; of sulphur as sulphate; of the total oxygen obtained by ignition, and of water.

To estimate the silver and sulphur, a weighed quantity was boiled with dilute hydrochloric acid until no more chlorine was evolved, and the whole of the black substance disappeared. The solution was then found to contain sulphuric acid, which was precipitated and weighed as barium sulphate after the silver chloride had been transferred to a Gooch crucible. That all the silver was thus converted to chloride was certain, since the same result was obtained by dissolving the original substance in dilute nitric acid, and then adding hydrochloric acid. The latter method was, however, unsuitable for the precipitation of barium sulphate, which then followed. Water was determined by weighing the original substance in a porcelain boat and heating it in a current of dry air in a combustion tube, which was packed at each end with ignited asbestos to prevent scattering. The water was collected and weighed in a U-tube containing sulphuric acid.

The estimation of the total oxygen expelled on heating was carried out in the following way. A weighed quantity of the substance was mixed with dry sand, and heated in a Jena-glass test-tube attached to a Toepler pump. As it decomposes explosively on heating, the test-tube was well packed with asbestos to prevent spitting. Before heating, the air was exhausted, and after heating, the total oxygen was drawn off and measured. Attempts were also made to estimate the amount of "available" oxygen by treating known quantities with potassium iodide solution and dilute sulphuric acid, and titrating the liberated iodine with sodium thiosulphate. The results obtained were, however, very variable, and therefore untrustworthy, since the available oxygen did not react quantitatively under these conditions:

0·7477 gave 0·7804 AgCl and 0·1801 BaSO<sub>4</sub>. Ag=78·57; SO<sub>4</sub>=9·90.  
 0·4970 „ 0·5179 AgCl „ 0·1203 BaSO<sub>4</sub>. Ag=78·44; SO<sub>4</sub>=9·95.  
 0·4452 „ 0·4682 AgCl „ 0·1067 BaSO<sub>4</sub>. Ag=79·14; SO<sub>4</sub>=9·85.  
 0·2646 „ 0·2772 AgCl. Ag=78·85.  
 0·2682 „ 0·0068 H<sub>2</sub>O. H<sub>2</sub>O=2·53.

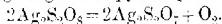
0·2080 „ 15·65 c.c. O<sub>2</sub> (dry) at 15·1° and 764 mm. O=10·25.  
 0·2561 „ 19·27 c.c. O<sub>2</sub> (dry) „ 14·7° „ 770 mm. O=10·34.

Mean: Ag=78·75; SO<sub>4</sub>=9·90; H<sub>2</sub>O=2·53; total oxygen expelled by heat=10·29 per cent.

#### *Interpretation of the Results.*

It may now be considered what light these results throw upon the constitution of the substance. That it is an oxidising agent is shown by its action on dilute hydrochloric acid, from which chlorine is liberated. Hence possible constituents are an oxide of silver, together with silver persulphate or silver sulphate. Now one would expect silver sulphate to remain unchanged on heating; hence the total oxygen expelled by heat would be derived from the oxide of silver. Theoretically 9·90 grams of SO<sub>4</sub> require 22·23 grams of silver for the formation of silver sulphate. Therefore we should have 56·52 grams of silver combined with 10·29 grams of oxygen; expressed in percentages, this gives Ag=81·58; O=15·40. Hence the atomic ratio obtained, namely, 1:1·228, is not a simple one.

On the other hand, if silver persulphate be present, it would lose oxygen on heating, giving silver pyrosulphate,



Now, 9·90 grams of SO<sub>4</sub> require 11·115 grams of silver to give 21·015 grams of silver persulphate, which, on heating, would lose 0·82 gram of oxygen. Hence, 78·75 - 11·12 = 67·63 parts of silver combine with 10·29 - 0·82 = 9·47 parts of oxygen; this gives Ag=87·7 and O=12·28 per cent., values which stand in the atomic ratio of 1·06:1, thus corresponding fairly well with the formula Ag<sub>2</sub>O<sub>2</sub>.

Evidently the latter view is the more reasonable, and accords well with the assumption made by Marshall (*loc. cit.*).

Under these conditions the results may be tabulated thus:

Ag = 78·75		
SO <sub>4</sub> = 9·90	(Ag <sub>2</sub> S <sub>2</sub> O <sub>8</sub> being the final product on heating Ag <sub>2</sub> S <sub>2</sub> O <sub>8</sub> )	
H <sub>2</sub> O = 2·53		
Total oxygen = 10·29		
	100·65	

We may therefore conclude that the specimen analysed contained approximately: Ag<sub>2</sub>S<sub>2</sub>O<sub>8</sub>=21; Ag<sub>2</sub>O<sub>2</sub>=77; H<sub>2</sub>O=2·5 per cent.

*Use of Silver Nitrate as a Catalytic Agent in Oxidations with Potassium Persulphate.*

I. *Oxidation of Toluene.*—The catalytic effect of silver nitrate is very pronounced in this case. Two parallel experiments were made under similar conditions for the sake of comparison, using a trace of silver nitrate in one case only. In each experiment, 10 grams of potassium persulphate (3 mols.) were dissolved in 120 c.c. of slightly warm distilled water. One gram of toluene (1 mol.) was added, and in one case 5 c.c. of  $N/10$ -silver nitrate solution. (This quantity of water proved to be insufficient to retain all the potassium persulphate in solution on cooling.) The flasks were corked, well shaken, and allowed to remain. In the one containing silver nitrate, the liquid quickly became turbid, then yellow; soon a yellow oil separated. On the following day this was extracted with ether. On evaporation of the ether, a yellow oil was obtained, which reduced silver nitrate, giving a mirror, and had the odour of benzaldehyde. Benzoic acid was also formed and was extracted by shaking some of the ethereal solution with dilute sodium hydroxide, and acidifying. Crystals were obtained, which on crystallisation from hot water melted at 119–120°.

In the other experiment, neither turbidity nor colour was observed, and on extracting with ether at the same time that the first was extracted, only unchanged toluene was found.

II. *Oxidation of Thymol.*

While the above experiments were in progress, a paper by Henderson and Boyd (Trans., 1910, **97**, 1659) appeared, in which it was stated that the oxidation of thymol in alkaline solution by potassium persulphate led only to tarry products, the bulk of the substance remaining unchanged, whereas hydrogen peroxide gave tetrahydroxycymene. This experiment was repeated with the persulphate, omitting the alkali and adding a trace of silver nitrate. Forty grams of potassium persulphate were dissolved in two litres of slightly warm water, and introduced into a flask with 20 grams of finely powdered thymol and 5 c.c. of  $N/10$ -silver nitrate. The mixture was allowed to remain for several days with frequent shakings. After a few hours, the solid turned brown. (In a parallel experiment without silver nitrate, no change was observed until after several weeks.)

After about a week the liquid was filtered off, the residue well shaken with dilute sodium hydroxide and ether, and the layers separated. The alkaline solution was acidified, and the precipitate allowed to crystallise once from ether, in which it was very soluble.

It was then recrystallised two or three times from benzene, from which it separated in needles melting at 162°. This substance is readily soluble in ether, ethyl acetate, acetone, or alcohol, but less so in benzene. Analysis and a determination of its molecular weight by the ebullioscopic method showed it to be dithymol, a substance first prepared by Dianin (*J. Russ. Phys. Chem. Soc.*, 1882, **14**, 135). (Found, C=80.11; H=9.23. — 0.2034, in 9.6 of ether, gave E=0.16; M.W.=286. Calc., C=80.53; H=8.72 per cent. M.W.=298.)

The etheral solution of the portion insoluble in alkali was evaporated. A brown solid remained, for which no crystallising medium could be found. Although insoluble in cold aqueous sodium hydroxide, it dissolved partly on prolonged heating. To ensure a better effect, it was dissolved in alcohol; sodium hydroxide was then added, and the mixture heated on the water-bath for half an hour. Steam was then blown through to expel the alcohol, and the liquid was filtered. On acidifying the filtrate, a small quantity of dithymol was obtained. The residue was again treated in a similar manner until no more substance would dissolve in alkali. The remainder was a brown, amorphous powder, which is possibly a polymerisation product.

The use of silver nitrate as a catalyst in oxidations of organic substances of various types is being further investigated.

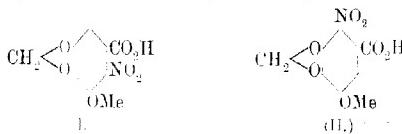
In conclusion, I desire to express my thanks to Professor Ingles for his kind interest in the work.

UNIVERSITY COLLEGE,  
READING.

XXXII.—*The Orientation of the Nitro-Group in Nitro-myristic acid.*

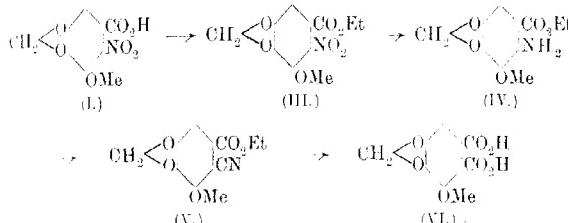
By ARTHUR HENRY SALWAY.

In a previous investigation (Trans., 1909, **95**, 1165) it was shown that myristicinic acid is converted by the action of cold concentrated nitric acid into a mixture of 5-nitro-1-methoxy-2:3-methylenedioxybenzene and nitromyristicinic acid. The position of the nitro group in the latter compound was not definitely established, there being two possible formulae, as represented by I and II:



The present investigation was therefore undertaken with the object of ascertaining which of these formulae must be assigned to the nitromyristicinic acid prepared in the above-mentioned reaction.

The method employed consisted in the conversion of the nitro-group of nitromyristicinic acid into a carboxylic group, when the product would be cotarnic acid (VI) or an isomeride, according as the constitution of nitromyristicinic acid is represented by formula I or II. This transformation was successfully accomplished according to the series of reactions represented below, and the final product was identified as cotarnic acid. Nitromyristicinic acid must therefore possess the constitution I, and is 6-nitro-5-methoxy-3:4-methylenedioxybenzoic acid:



The determination of the position of the nitro-group in nitromyristicinic acid establishes, in addition, the constitutions of nitromyristicinaldehyde (*loc. cit.*, p. 1160), and of a series of synthetic products derived from the latter compound\* (*Trans.*, 1909, **95**, 1294).

#### EXPERIMENTAL.

For the purpose of this investigation it was necessary to prepare a considerable quantity of nitromyristicinic acid. The method already described for the preparation of this compound (*Trans.*, 1909, **95**, 1165) is unsatisfactory, since approximately 60 per cent. of the myristicinic acid is converted into 5-nitro-1-methoxy-2:3-methylenedioxybenzene by elimination of carbon dioxide. It has now been found, however, that by esterification of the myristicinic acid prior to nitration the secondary change is entirely avoided.

These compounds comprise: *ω*-2-dinitro-3-methoxy-1:5-methylenedioxy-styrene; 2-nitro-3-methoxy-4:5-methylenedioxycinnamic acid; 2-amino-3-methoxy-1:5-methylenedioxycinnamic acid; 2-keto-8-methoxy-6:7-methylenedioxy-1:2-dihydroquinoline; 8-methoxy-6:7-methylenedioxycarboxyethyl methyl ether; 2-keto-8-methoxy-1-methyl-6:7-methylenedioxy-1:2-dihydroquinoline and oxy/secotarnine.

*Ethyl Nitromyristinate (Ethyl 2-Nitro-3-methoxy-4: 5-methylenedioxybenzoate), III, p. 267.*

Twenty grams of ethyl myristinate (b. p. 193°/20 mm.) were added gradually at 0° to 200 c.c. of concentrated nitric acid (D 1·41). The mixture was kept in the cold for an hour, and then poured into ice-water, when an oil was precipitated, which gradually solidified. This was collected, washed free from nitric acid, and purified by recrystallisation from alcohol. The compound was thus obtained in stout, colourless prisms, melting at 82°:

0·4019 required for saponification 15·05 c.c. N/10 NaOH.  
Saponification value = 210·1.

$C_{11}H_{11}O_5N$  requires saponification value = 208·6.

*Ethyl nitromyristinate* is colourless when freshly prepared, but gradually becomes yellow on exposure to light. When hydrolysed, it yields a mononitromyristinic acid, which was proved to be identical with the acid derived by the direct nitration of myristinic acid.

*Ethyl Aminomyristinate (Ethyl 2-Amino-3-methoxy-4: 5-methylenedioxybenzoate), IV, p. 267.*

For the preparation of this compound, one part of ethyl nitromyristinate was cautiously heated with tin (one part) and an excess of concentrated hydrochloric acid. After the vigorous reaction had subsided and the nitro-ester had completely dissolved, the mixture was poured into a large volume of water, when the greater portion of the amino-ester was precipitated as an oil, which soon became solid. This was collected, washed, and purified by recrystallisation from alcohol. A further quantity of the amino-ester was obtained from the acid filtrate by rendering it alkaline and extracting with ether:

0·1114 gave 0·2250 CO<sub>2</sub> and 0·0546 H<sub>2</sub>O. C = 55·1; H = 5·4.  
 $C_{11}H_{12}O_5N$  requires C = 55·2; H = 5·4 per cent.

*Ethyl aminomyristinate* crystallises from alcohol in colourless prismatic needles, melting at 93°. Its ethereal solution possesses a blue fluorescence. It is a very weak base, being precipitated from its solution in concentrated hydrochloric acid by the addition of water. When hydrolysed, it yields aminomyristinic acid, which crystallises from alcohol in long, slender, colourless needles, melting and decomposing at 200°. Solutions of the latter substance also show a blue fluorescence:

0·1190 gave 0·2239 CO<sub>2</sub> and 0·0480 H<sub>2</sub>O. C = 51·3; H = 4·5.  
 $C_8H_8O_5N$  requires C = 51·2; H = 4·5 per cent.

*Ethyl Cyanomyristicinate* (*Ethyl 2-Cyano-3-methoxy-4:5-methylene-diarylbenzoate*), V, p. 267.

Ethyl aminomyristicinate was dissolved in rather more than two molecular proportions of hot sulphuric acid (10 per cent.), and the solution cooled, with vigorous agitation. A solution of sodium nitrite (1 mol.) was slowly added at 0°. After some time the mixture was filtered to remove unchanged amino-ester, and the filtrate added in small portions to a hot solution of cuprous cyanide. The mixture was heated on the boiling-water bath for an hour, then cooled, and extracted with ether. The ethereal extract was washed first with sodium hydroxide, which removed some resinous matter, and then with water. On removing the solvent, the residue soon solidified; it was purified by crystallisation from alcohol, and thus obtained in yellow prisms, melting at 111°.

0.1252 gave 0.2652 CO<sub>2</sub> and 0.0534 H<sub>2</sub>O. C=57.8; H=4.7.  
C<sub>10</sub>H<sub>12</sub>O<sub>3</sub>N requires C=57.8; H=4.4 per cent.

*Ethyl cyanomyristicinate* is readily soluble in benzene, chloroform, or ether, but only moderately so in cold alcohol. When heated for a short time with alcoholic potassium hydroxide, it is converted into *cyanomyristicinic acid*, which crystallises from alcohol in prismatic needles, melting at 221°.

*Cotarnic Acid*, VI, p. 267.

In order to prepare cotarnic acid from ethyl cyanomyristicinate, the latter was heated with an excess of alcoholic potassium hydroxide until ammonia ceased to be evolved. After removing the alcohol, the alkaline liquid was acidified with dilute hydrochloric acid, and then extracted with ether. The ethereal solution yielded a crystalline residue, which was recrystallised from benzene containing a little methyl alcohol. It was thus obtained in colourless, square prisms, decomposing at 178° with the formation of an anhydride, which then melted at 160° (0.0990 required 8.25 c.c. 3 N KOH for neutralisation. M.W.=240. C<sub>8</sub>H<sub>6</sub>O<sub>3</sub>(CO<sub>2</sub>H)<sub>2</sub> requires M.W.=240).

It is evident that the above substance possesses the composition and properties of cotarnic acid. Its identity was further confirmed by conversion into the methylimide of cotarnic acid. This was prepared by dissolving the cotarnic acid in an excess of methylamine solution, evaporating to dryness, and subjecting the methylamine salt to destructive distillation under diminished pressure (compare Perkin, Robinson, and Thomas, Trans., 1909, 95, 1984). The distillate solidified at once, and on recrystallisation from alcohol was

obtained in colourless needles. When heated in a capillary tube the methylimide began to change about 186°, and completely melted at 199° with partial volatilisation. (Found, C=56·5; H=4·1. Calcd., C=56·2; H=3·8 per cent.)

For purposes of comparison, a specimen of the methylimide of cotarnine acid was prepared by the oxidation of cotarnine (Freund and Wulff, *Ber.*, 1902, **35**, 1739). This product also began to change at about 186°, and melted completely at 199°, whilst admixture with the synthetic methylimide produced no change in the point of fusion. Freund and Wulff \* (*loc. cit.*) attribute to the methylimide of cotarnine acid a melting point of 205—206°, but the present author, as seen above, has not been able to confirm this observation.

THE WELLCOME CHEMICAL RESEARCH LABORATORIES,  
LONDON, E.C.

### XXXIII.—*The Synthesis of 3- $\beta$ -Aminoethylindole.*

By ARTHUR JAMES EWINS.

A very considerable amount of interest has of late centred round a number of amines which may be considered to belong to a special group in that they are derived from the amino-acids of protein by the removal of carbon dioxide (loss of the carboxyl group). Such bases are often produced by the action of putrefactive organisms on the amino-acids.

The earliest examples of this class of bases were discovered by Brieger in the ptomaines, putrescine and cadaverine. Their formation by the action of putrefactive organisms on the corresponding amino-acids was first established by Ellinger (*Ber.*, 1899, **32**, 3542). Since then amines derived from almost all the known amino-acids have been obtained either by putrefactive processes or by chemical means. The interest attaching to these bases lies in the fact that certain of the more complex amines are possessed of considerable physiological activity, and have been the subject of several recent communications (Barger and Walpole, *J. Physiol.*, 1909, **38**, 343; Dale and Dixon, *J. Physiol.*, 1909, **39**, 25; Acker-

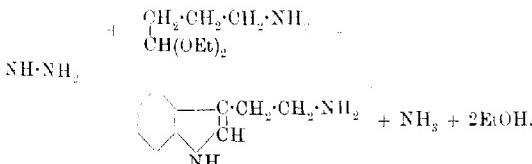
\* Since writing the above the author has received a private communication from Dr. M. Freund stating that the melting point previously ascribed to the methylimide of cotarnine acid is incorrect. A specimen of this substance kindly sent by Dr. Freund, to whom the author desires to express his sincere thanks, melted at 199° and was identical with the compound described in this investigation.

mann and Kutschner, *Zeitsch. Biol.*, 1910, **54**, 387; Barger and Dale, *Trans.*, 1910, **97**, 2592; Dale and Laidlaw, *J. Physiol.*, 1910, **41**, 318).

Of the amino-acids known to occur in proteins for which the corresponding amine remained unknown, tryptophan is the most important. This amino-acid was first isolated by Hopkins and Cole (*J. Physiol.*, 1901-1902, **27**, 418), and afterwards synthesised by Ellinger and Flamand (*Ber.*, 1907, **40**, 3029). The amine derived from this amino-acid has now been obtained both synthetically and by the action of putrefactive bacteria on tryptophan itself (Ewins and Laidlaw, *Proc.*, 1910, **26**, 343), and the method of synthesis forms the subject of the present communication. (The action of putrefactive bacteria on tryptophan had previously been studied, but the isolation of the base was achieved only when its synthesis had revealed the properties of the amine.)

It was at first hoped that by heating tryptophan under very greatly diminished pressure, carbon dioxide might be split off, as in the case of tyrosine. This experiment was carried out at Dr. G. Barger's suggestion but the only product that could be isolated from the sublimate was a very small quantity of unchanged tryptophan. The method employed by Windaus and Vogt (*loc. cit.*) in the synthesis of 4- $\beta$ -aminoethylglyoxaline from  $\beta$ -glyoxaline-4-propionic acid derived from histidine cannot here be employed, owing to the action of nitrous acid on the indole nucleus.

The method ultimately adopted was a modification of Fischer's method of synthesising indole derivatives, in which the phenyl-hydrazone of the suitable aldehyde is heated with zinc chloride. In this instance, the requisite aldehyde cannot be isolated in the free state on account of the readiness with which condensation takes place with formation of cyclic compounds (Wohl and Schäfer, *Ber.*, 1905, **38**, 4157). It was found, however, that the corresponding acetal ( $\gamma$ -aminobutyryl acetal) could be employed in place of the aldehyde, and that by heating with zinc chloride and phenyl-hydrazine, condensation was effected, alcohol and ammonia being eliminated, and a good yield of the desired base thus obtained. The reaction may be represented thus:

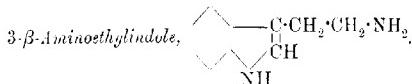


The picrate of the base was found to be identical in all respects,

chemical and physiological, with that of the base obtained by the action of putrefactive bacteria on tryptophan. This fact, the method of formation, and the analytical results leave no doubt as to the constitution of the base. As might be expected, the base gives the glyoxylic (Adamkiewicz) reaction described in detail by Hopkins and Cole (*Proc. Roy. Soc.*, 1901, **68**, 21) as a reaction for tryptophan. With bromine, however, which with tryptophan gives a pink colour, no reaction is obtainable.

As was expected, the base proved to be physiologically active. Dr. P. P. Laidlaw, who is undertaking its physiological examination, and by whom a full account of its action will be communicated elsewhere, has found that among other effects it produces a rapid and marked rise of blood pressure.

#### EXPERIMENTAL.



Four grams of  $\gamma$ -aminobutyrylacet al (b. p. 104–106°/18 mm.), obtained according to the method employed by Wohl and Schäfer (*Ber.*, 1901, **34**, 1911), were heated to 180° for three hours with 2·6 grams of phenylhydrazine and 3·6 grams of anhydrous zinc chloride in an open vessel. The product was dissolved in dilute acetic acid, the solution extracted with ether, and the zinc removed from the acetic acid solution as sulphide. The filtrate was then concentrated under diminished pressure to about 10 c.c. On cooling, a crystalline precipitate separated, which was collected. The crude hydrochloride thus obtained was dissolved in a small quantity of water, and an excess of an aqueous solution of sodium hydroxide added. An oil separated which, on keeping, crystallised to a mass of fine needles. The base thus obtained was recrystallised from a mixture of alcohol and benzene, and separated in long, colourless needles, melting at 145–146°. Yield, 45 per cent. of the theoretical:

0·1100 gave 0·3862 CO<sub>2</sub> and 0·0960 H<sub>2</sub>O. C=75·2; H=7·5.

C<sub>10</sub>H<sub>12</sub>N<sub>2</sub> requires C=75·0; H=7·5 per cent.

3- $\beta$ -Aminoethylindole is readily soluble in alcohol or acetone, and almost insoluble in water, ether, benzene, or chloroform. The base decomposes on heating under the ordinary pressure, yielding volatile products having an indole-like odour.

The free base (as well as its salts) gives the bluish-violet coloration with glyoxylic acid and concentrated sulphuric acid described by Hopkins and Cole (*loc. cit.*) as a characteristic reaction of tryptophan. The reaction may be obtained with a solution of one part of the base in about 300,000 parts. With bromine, however,

no coloration is obtained, the base differing in this respect from tryptophan, which gives a pink colour.

*3- $\beta$ -Aminoethylindole Hydrochloride*,  $C_{10}H_{12}N_2 \cdot HCl$ .

The crude hydrochloride of 3- $\beta$ -aminoethylindole, obtained as described above, was recrystallised from 95 per cent. alcohol by careful addition of ether. The salt was thus obtained in colourless, thin prisms, melting at 246°;

$nD^{20} = 1.44$  gave 0.1058 AgCl. Cl = 18.1.

$C_{10}H_{12}N_2 \cdot HCl$  requires Cl = 18.1 per cent.

The hydrochloride is soluble in about 12 parts by weight of water at 18°, and very soluble in hot water, from which it may be recrystallised.

*3- $\beta$ -Aminoethylindole Picrate*,  $C_{10}H_{12}N_2 \cdot C_6H_2(NO_2)_3 \cdot OII$ .

This salt, the most characteristic of the base, is readily obtained by addition of a cold saturated aqueous solution of picric acid to a solution of the hydrochloride in water. The mixture immediately becomes turbid and orange-red in colour, and dark red crystals, consisting of fern-like aggregates of needles or prisms (very similar in form to that of ammonium chloride), rapidly separate. The picrate is characterised by its general insolubility. It is almost insoluble in water, very sparingly soluble in alcohol, ethyl acetate, chloroform, and most organic solvents except acetone, in which it is readily soluble.

For analysis, the salt was recrystallised from dilute acetone. The pure picrate melted and decomposed at 242—243°;

$0.1286$  gave 0.2338 CO<sub>2</sub> and 0.0452 H<sub>2</sub>O. C = 49.6; H = 3.9.

$C_{10}H_{11}O_7N_3$  requires C = 49.3; H = 3.85 per cent.

*3- $\beta$ -Aminoethylindole picrolonate* was prepared by adding rather more than one molecular proportion of picrolonic acid in dilute alcoholic solution to an aqueous solution of the hydrochloride. On concentrating the mixture, a crystalline solid separated, which was readily recrystallised from hot water, and separated in bundles of short, stout, deep chrome-yellow prisms, melting and decomposing at 231°.

The *benzoyl* derivative, obtained by the Schotten-Baumann method, or by heating the base with benzoic anhydride, is not readily obtained crystalline. It may be crystallised by very slow evaporation of the alcoholic solution of the compound, or by very careful addition of light petroleum to its solution in dry ether or ethyl acetate, and is then obtained in stout prisms, melting at 137—138°.

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HERNE HILL, S.E.

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## ERRATA.

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Page	Line
1468	11 <sup>a</sup> and 12 <sup>b</sup> for "analysis read";
0·2801	gave 0·6353 CO <sub>2</sub> and 0·1850 H <sub>2</sub> O. C=61·86; H=7·33. C <sub>6</sub> H <sub>14</sub> O <sub>2</sub> N <sub>2</sub> requires C=61·9; H=7·2 per cent.

## ANNUAL REPORTS, VOL. VII (1910).

83 11<sup>a</sup> and 12<sup>b</sup> for "a racemic compound is not formed in these cases" for  
"the solubility method fails in these cases to indicate whether  
a racemic compound is formed or not."

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Page	Line
ii, 216	5 <sup>a</sup> for "unmanilled" read "manilled."
ii, 248	17 <sup>a</sup> "von Roth" read "von Rath."
ii, 589	8 <sup>a</sup> "venote" "sodalite."
ii, 745	13 <sup>a</sup> <i>inscri</i> "Rhodesia" before "Broken Hill."
ii, 745	8 <sup>a</sup> for "orthorhombic" read "anorthic."
ii, 745	7 <sup>a</sup> <i>raser</i> "optic" before "axial angle."
ii, 1926	16 <sup>a</sup> for "Corinth" read "Carinthia."

## VOL. XC VIII (ABSTR., 1910).

ii, 46	17 for "Er <sub>2</sub> O <sub>3</sub> " read "Bi <sub>2</sub> O <sub>3</sub> "
ii, 137	111 "granite" "garnet."
ii, 137	141 " " "
ii, 312	16 " " 210" read "221."
ii, 967	23 " " amorphous" read "isomorphous."
ii, 968	4 " " kannemerite" read "kannemeyerite."
ii, 968	10 " " R <sub>2</sub> Si <sub>2</sub> O <sub>5</sub> SiO <sub>4</sub> " read "R <sub>2</sub> R' <sub>2</sub> Si <sub>2</sub> O <sub>5</sub> "
ii, 969	20 " " Rhenish" read "Rhenish."

## VOL. C (ABSTR., 1911).

i,	36 20 <sup>a</sup> for "462" read "174."
i,	116 21 for "glycol" read "glycine."
i,	73 15 for "GOEBEL" read "GAEBEL."

\* From bottom.

no coloration is obtained, the base differing in this respect from tryptophan, which gives a pink colour.

*3- $\beta$ -Aminoethylindole Hydrochloride*,  $C_{10}H_{12}N_2\cdot HCl$ .

The crude hydrochloride of 3- $\beta$ -aminoethylindole, obtained as described above, was recrystallised from 95 per cent. alcohol by careful addition of ether. The salt was thus obtained in colourless, thin prisms, melting at 246°:

$\sigma 1441$  gave 0·1058 AgCl. Cl = 18·1.

$C_{10}H_{12}N_2\cdot HCl$  requires Cl = 18·1 per cent.

The hydrochloride is soluble in about 12 parts by weight of water at 18°, and very soluble in hot water, from which it may be recrystallised.

*3- $\beta$ -Aminoethylindole Picrate*,  $C_{10}H_{12}N_2C_6H_2(NO_2)_3\cdot OH$ .

This salt, the most characteristic of the base, is readily obtained by addition of a cold saturated aqueous solution of picric acid to a solution of the hydrochloride in water. The mixture immediately becomes turbid and orange-red in colour, and dark red crystals, consisting of fern-like aggregates of needles or prisms (very similar in form to that of ammonium chloride), rapidly separate. The picrate is characterised by its general insolubility. It is almost insoluble in water, very sparingly soluble in alcohol, ethyl acetate, chloroform, and most organic solvents except acetone, in which it is readily soluble.

For analysis, the salt was recrystallised from dilute acetone. The pure picrate melted and decomposed at 242–243°:

$\sigma 1286$  gave 0·2338 CO<sub>2</sub> and 0·0152 H<sub>2</sub>O. C = 49·6; H = 3·9.

$C_{10}H_{12}O_7N_3$  requires C = 49·3; H = 3·85 per cent.

*3- $\beta$ -Aminoethylindole picrolonate* was prepared by adding rather more than one molecular proportion of picrolic acid in dilute alcoholic solution to an aqueous solution of the hydrochloride. On concentrating the mixture, a crystalline solid separated, which was readily recrystallised from hot water, and separated in bundles of short, stout, deep chrome yellow prisms, melting and decomposing at 231°.

The *benzoyl* derivative, obtained by the Schotten-Baumann method, or by heating the base with benzoic anhydride, is not readily obtained crystalline. It may be crystallised by very slow evaporation of the alcoholic solution of the compound, or by very careful addition of light petroleum to its solution in dry ether or ethyl acetate, and is then obtained in stout prisms, melting at 137–138°.

THE WELLCOME PHYSIOLOGICAL RESEARCH LABORATORIES,  
HEENE HILL, S.E.

XXXIV.—*The Colour and Constitution of Bromine Solutions.*

By ALFRED FRANCIS JOSEPH and JAMES NADORIS JINENDRADASA

If a soluble bromide is added to bromine water, the colour of the solution is greatly diminished, the effect depending to some extent on the amount of bromide added, and it was thought that a quantitative examination of such colour changes might afford additional evidence for the constitution of bromine solutions which has been adduced from the study of their other properties. The experiments of Worley (Trans., 1905, 87, 1107) confirmed the views of previous workers, that a considerable part of the bromine was in the form of tribromide, and he found values for the dissociation constant in the equation :

$$k(\text{KBr}_3) = (\text{KBr}) \times (\text{Br}_2)$$

varying from 0·03 to 0·07, the variation being probably due to the presence of a portion of the bromine in the form of pentabromide.

The experiments recorded in this paper have led to a similar result, and have been extended to sodium bromide and hydrobromic acid; the presence of the compounds  $\text{NaBr}_3$  and  $\text{HBr}_3$  is similarly to be inferred, the dissociation constants of these being practically the same as that of the compound  $\text{KBr}_3$ .

The method adopted consisted of finding the strengths of bromine and bromine-bromide solutions having the same intensity of colour.

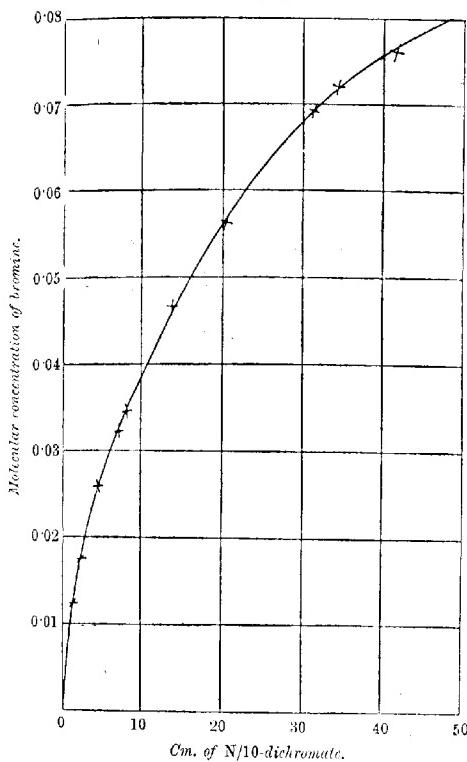
Experiments with the colorimeter on bromine solutions are complicated by rapid loss of bromine from the surface when contained in an open vessel, and consequent lack of homogeneity of the liquid. It is essential that the liquid should be contained in a covered vessel which it completely fills, to enable concordant results to be obtained.

In comparing colours of the solutions, it was thus difficult to use standard bromine solutions the depth of which could be varied at will, and it became necessary to work with a third non-volatile substance, first with bromine water and then with bromine in potassium bromide; in this way, a relation could be obtained between the two latter.

A Duboscq colorimeter was used for the comparisons. In this instrument good diffused daylight reflected from a porcelain plate passes up through two vessels containing the liquids to be compared. A hollow glass cylinder closed at both ends dips into the standard

liquid, and by moving this up or down, the thickness of the layer of liquid between the bottoms of the containing vessel and hollow cylinder can be varied and read off on a scale. The two beams of light, after passing through the liquids, are reflected by prisms so as to illuminate the two halves of the field of an eye-piece.

FIG. 1.



The non-volatile substance used was potassium dichromate, which was chosen on account of the ease with which standard solutions are prepared and kept, and because it can be well matched against bromine.

The standard solutions of dichromate used were  $2N$ ,  $N$ ,  $N/2$ ,  $N/5$ , and  $N/10$ . These are optically equivalent, that is, 4 cm. of a  $N/2$ -solution are matched by 1 cm. of a  $2N$ -solution, etc.

Bromine and potassium dichromate are not, however, optically equivalent. Their absorption spectra differ, that of the bromine extending further into the red, and ending much less sharply than that of dichromate. Further, if two oblong vessels be filled with bromine and dichromate respectively, so that the colours match when viewed through their long dimensions, the bromine appears far lighter when viewed through their short dimensions.

It has been found that this does not affect the final result, the dichromate being only introduced at an intermediate stage in order to effect comparison between the two bromine solutions.

The first part of the work consisted of comparing the colour of aqueous bromine of various strengths with potassium dichromate solutions, and from the results constructing a calibration curve by plotting strengths of bromine as abscissæ against cm. of N/10-dichromate as ordinates.

*Calibration Curve Showing the Relation between the Strength of Bromine contained and the depth in cm. of N/10-Dichromate equivalent in colour.*

The bromine was contained in a glass vessel about 2·7 cm. diameter and 1·7 cm. high, the top edge being ground and covered by a clear glass disk. The volume of the vessel was found by weighing to be 9·5 c.c.

The cell was filled with bromine water, and the colour matched with suitable dichromate. It was then dropped into potassium iodide, and the liberated iodine titrated with standard thiosulphate, whereby the molecular concentration of the bromine solution was determined.

TABLE I.  
*Construction of Calibration Curve.*

Standard bi- chromate used.	Colorimeter readings.	Mean.	Colour of di- chromate in bromine water.	Molecular concen- tration of bromine in cm. N/10.
N/10	1·18, 1·20, 1·20, 1·18, 1·14, 1·18	1·17	1·17*	0·012
N/5	1·19, 1·16, 1·17, 1·13, 1·18, 1·15	1·16	2·32	0·017
N/5	2·23, 2·18, 2·23, 2·18, 2·20, 2·21	2·23	4·46	0·028
N/2	1·47, 1·49, 1·41, 1·36, 1·45, 1·49	1·44	7·20	0·033
N/2	1·60, 1·68, 1·64, 1·69, 1·55, 1·62	1·63	8·18	0·037
N	1·39, 1·38, 1·39, 1·43, 1·40, 1·46	1·39	13·9	0·044
N	2·14, 2·01, 2·02, 2·08, 2·01, 2·04	2·05	20·6	0·056
2N	1·58, 1·56, 1·50, 1·67, 1·55, 1·50	1·56	31·2	0·068
2N	1·75, 1·70, 1·67, 1·80, 1·75, 1·65	1·72	34·4	0·0720
2N	2·10, 2·11, 2·06, 2·04, 1·99, 2·18	2·09	41·8	0·0758
2N	2·78, 2·56, 2·83, 2·64, 2·56, 2·81	2·70	54·0	0·0845

\* The mean multiplied by ten times the normality factor gives the colour in cm. of N/10-dichromate.

The last two columns plotted give the calibration curve shown in Fig. 1 (p. 275).

*Comparison of the Strengths of Solutions of Bromine in Water and in Aqueous Potassium Bromide, having the same colour.*

A solution of bromine in potassium bromide solution of the required strength was placed in the cell and matched against a suitable dichromate solution. By means of the calibration curve, the strength of bromine water having the same colour was read off, and this was taken as the colour of the bromine-bromide solution, the unit of colour being that of aqueous bromine containing 1 grammolecule per litre. The concentration of the bromine in the solution under examination was determined as before with potassium iodide and standard thiosulphate.

Only the mean of the colorimeter readings is given here, the agreement being of the same order as that shown by the calibration figures. At least six readings were made for each determination.

TABLE II.  
*Influence of Potassium Bromide on the Colour.*

Molecular concentration of potassium bromide.	Standard dichromate used.	Mean colorimeter reading.	Colour expressed in strength of $\text{Br}_2$ (from the calibration curve).	Bromine concentration (from the titration).
0·1	N/10	1·83	0·015	0·0255
0·1	N/5	1·29	0·018	0·0305
0·1	N/2	2·12	0·040	0·0620
0·1	N	1·51	0·0185	0·0712
0·1	2N	1·94	0·075	0·1071
0·4	N/5	2·58	0·027	0·0665
0·4	N/2	1·18	0·029	0·0708
0·4	N	1·09	0·041	0·0984
0·4		1·77	0·053	0·1239
0·4	2N	0·98	0·056	0·1305
0·4	2N	2·26	0·0785	0·1835
1·0	N/5	1·34	0·018	0·0547
1·0	N/2	1·05	0·027	0·0839
1·0	2N	0·45	0·037	0·1082
1·0	2N	1·10	0·0555	0·1811
1·0	N	2·13	0·0575	0·1830
1·0	2N	1·57	0·060	0·2050
1·0	2N	2·10	0·0765	0·2362
1·0	2N	2·38	0·0795	0·2592

The last two columns are plotted in Fig. 2, the colour of bromine water being shown as a straight line with equal ordinates and abscisse.

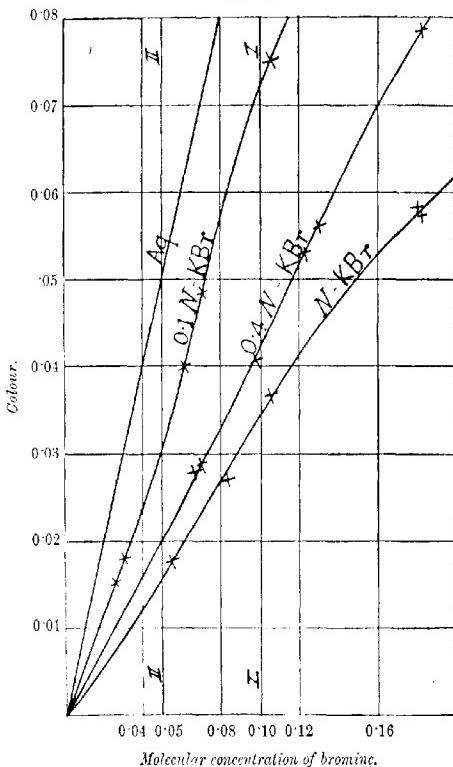
A vertical line drawn across the diagram gives the colours of solutions having the same bromine concentration, and the numbers so obtained show the effect of increasing the concentration of the

potassium bromide on the colour of a bromine solution of fixed strength.

Thus, at line 1, where concentration of bromine is

0·1, when the conc. of KBr is 0·1, 0·4, 1·0  
the colour is 0·07, 0·0415, 0·034,

FIG. 2.



and at line 2, where concentration of bromine is

0·05, when the conc. of KBr is 0·1, 0·4, 1·0  
the colour is 0·032, 0·02, 0·016.

These numbers indicate clearly that whilst the addition of a small quantity of bromide causes a very marked falling off in the intensity of the colour, continued addition produces far less effect, and after

the concentration of potassium bromide has reached about 0·8, further addition produces little change.

As a further example, a solution of 0·204 molecular proportion of bromine in *N*-potassium bromide had a colour 0·065, whilst in 2*N*-potassium bromide the colour was 0·062; doubling the concentration of the bromide has thus little effect on the colour.

Colour change in solution may be caused by increase or decrease of electrolytic dissociation or change in constitution (compare Sidgwick and Tizard, *Trans.*, 1908, **93**, 187).

Since Jakowkin (*Ber.*, 1897, **30**, 518) found that bromine water cannot be ionised to any considerable extent, the addition of a soluble bromide could hardly increase its dissociation.

A few experiments were made with the view of determining the effect of the addition of bromine on the conductivity of potassium bromide solutions, and it was found that at 25° the addition to 0·4*N*-potassium bromide of 0·2 gram-molecule of bromine per litre lowers its conductivity about 8 per cent., 0·2 gram-molecule per litre of the non-electrolyte sugar lowering it about 12 per cent. The lowering may be due to viscosity changes, and is in harmony with the view that no great change in ionic concentration is caused by the addition of the bromine.

The colour changes must therefore almost certainly be due to some change of constitution, the simplest of which would be the formation of the compound  $\text{KBr}_3$ .\*

In the simple treatment that follows, it is assumed that the limit of colour change is reached in normal potassium bromide solution. It is further assumed that potassium tribromide is the only additive compound the presence of which need be considered.

If, then, after this concentration has been reached, further addition of potassium bromide produces no effect, the whole of the bromine must be in the combined state, and the colour of the solution in *N*-potassium bromide (within the limits of bromine concentration here dealt with) is due to potassium tribromide, and not to free bromine.

Consider a solution of bromine in potassium bromide, the total concentration of the dissolved bromine being  $a$ . Let its colour be  $C$ . Further, let the colour of a solution of potassium tribromide (that is, bromine in *N*-potassium bromide) of molecular concentration  $a$  be  $P$ . Then, in the solution under discussion, the colour is due partly to free bromine (say, concentration  $r$ ) and partly to

\* The formation of  $\text{Br}_3^+$  ions would be attended by diminution of conductivity owing to their probably having lower mobility. Bray and Mackay (*J. Amer. Chem. Soc.*, 1910, **32**, 919) have shown the diminution in conductivity brought about by dissolving iodine in aqueous potassium iodide, and caused by the lower mobility of the  $\text{I}_3^-$  ion.

potassium tribromide ( $a - x$ ). Now, assuming that decrease in colour is proportional to the amount of potassium tribromide formed, then the colour of a solution of  $a$  gram-mol Br

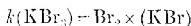
when conc. of free Br is  $P$  is  $P$

$$\begin{array}{cccccc} " & " & " & " & x & , \\ " & " & " & " & a & \text{(that is, } \text{Br}_2\text{Aq}) \text{ is } a, \end{array}$$

so that proportionally

$$a = \frac{a - P}{c - P} \text{ or } x = \frac{a(c - P)}{a - P}$$

The concentration of the free bromine being thus found, that of the potassium tribromide is  $a - x$ . This, subtracted from the total potassium bromide concentration, gives the uncombined potassium bromide. From these the dissociation constant in the equation:



can then be calculated.

The value of  $k$  is shown for the experiments of table II. The numbers in the first three columns are taken from table II. Those in the fourth are taken from the  $N$ -potassium bromide curve in Fig. 2.

TABLE III.

## Dissociation Constant of Potassium Tribromide.

Total concen- tration, KBr	Colour of KBr <sub>3</sub> solution of concen- tration of KBr <sub>3</sub>	Colour of KBr <sub>2</sub>				Free KBr = $(a - x)$	$\frac{1}{k}$
		Total concen- tration, KBr	Colour of KBr <sub>3</sub>	Free Br = $x$	KBr <sub>3</sub> total KBr = $a - x$		
0.1	0.0255	0.015	0.0078	0.0101	0.0151	0.0849	0.053
0.1	0.0365	0.018	0.0095	0.0123	0.0182	0.0818	0.055
0.1	0.0620	0.040	0.0198	0.0297	0.0523	0.0567	0.059
0.1	0.0712	0.045	0.0236	0.0379	0.0333	0.0667	0.054
0.1	0.1071	0.075	0.0372	0.0579	0.0492	0.0508	0.060
0.1	0.0665	0.027	0.0212	0.0085	0.0580	0.3420	0.050
0.1	0.0708	0.029	0.0225	0.0095	0.0613	0.3687	0.057
0.1	0.0981	0.041	0.0332	0.0115	0.0866	0.3131	0.041
0.1	0.1239	0.053	0.0431	0.0152	0.1087	0.2913	0.041
0.1	0.1305	0.056	0.0458	0.0157	0.1148	0.2852	0.040
0.1	0.1835	0.075	0.0628	0.0239	0.1596	0.2464	0.056

In taking the colour of the potassium tribromide solutions from Fig. 2, the smoothed curve has not been used, but each pair of consecutive points has been joined by straight lines. The values of  $k$  obtained in this way are of the same order of magnitude and constancy as those obtained by Worley, the variations being from 0.03 to 0.07.

A large number of determinations were made to see whether

sodium and hydrogen bromides behaved in the same way, and from the examples given in the next tables it will be seen that the results are quite similar.

TABLE IV.

*Dissociation Constant of Sodium Tribromide.*

Concen- tration NaBr.	Total Br = $a$ .	Colour $C$ .	Colour $a = P$ .	Colour of NaBr <sub>3</sub> solution	concen- tration Br = $x$ .	Free NaBr <sub>3</sub>	Free NaBr = total NaBr.	$k$ .
0·1	0·0519	0·036	0·020	0·0260	0·0258	0·0258	0·0711	0·071
0·1	0·0659	0·046	0·0255	0·0327	0·0362	0·0368	0·065	0·065
0·1	0·0805	0·055	0·0295	0·0402	0·0403	0·0597	0·060	0·060
0·1	0·1110	0·077	0·030	0·0580	0·0530	0·0470	0·052	0·052
0·1	0·0127	0·019	0·0165	0·0041	0·0036	0·0014	0·0301	0·038
0·1	0·0762	0·032	0·028	0·0063	0·0069	0·0001	0·3207	0·034
0·1	0·0866	0·0368	0·0315	0·0083	0·0783	0·0001	0·2947	0·045
0·1	0·1214	0·053	0·0425	0·0161	0·1053	0·0001	0·2541	0·045
0·1	0·1720	0·077	0·060	0·0261	0·1459	0·0001	—	—
1·0	0·623	0·013	—	—	—	—	—	—
1·0	0·647	0·024	—	—	—	—	—	—
1·0	0·1037	0·0375	—	—	—	—	—	—
1·0	0·1415	0·049	—	—	—	—	—	—
1·0	0·1824	0·0685	—	—	—	—	—	—
1·0	0·2440	0·076	—	—	—	—	—	—

TABLE V.

*Dissociation Constant of Hydrogen Tribromide.*

Concen- tration HBr.	Total Br = $a$ .	Colour $C$ .	Colour $a = P$ .	Colour of HBr <sub>3</sub> solution	concen- tration Br = $x$ .	Free HBr <sub>3</sub>	Free HBr = total HBr.	$k$ .
0·1	0·060	0·039	0·020	0·0285	0·0315	0·0855	0·062	0·062
0·1	0·090	0·062	0·031	0·0473	0·0427	0·0573	0·064	0·064
0·1	0·065	0·027	0·022	0·0098	0·0552	0·3448	0·061	0·061
0·1	0·133	0·055	0·046	0·0191	0·1130	0·2861	0·048	0·048
1·0	0·042	0·015	—	—	—	—	—	—
1·0	0·079	0·027	—	—	—	—	—	—
1·0	0·107	0·037	—	—	—	—	—	—
1·0	0·149	0·052	—	—	—	—	—	—
1·0	0·188	0·0635	—	—	—	—	—	—

If curves exhibiting the relation between bromine concentration and colour are plotted, they are found to be almost coincident with the corresponding ones for potassium bromide, the values for  $k$  being likewise practically the same.

*Summary.*

- Bromides lighten the colour of aqueous bromine solution, the diminution depending on the amount of bromide added. The

results obtained with sodium, potassium, and hydrogen bromides are similar.

2. After the concentration of the bromide has reached normal, further addition produces little effect on the colour. It is therefore assumed that in such solutions practically the whole of the bromine is in the combined state.

3. In bromide solutions of concentration less than normal, the colour is due partly to free and partly to combined bromine, the amounts of which can be calculated with the aid of the curves.

4. Application of the law of mass-action to the results supports the view that the principal reaction causing the colour change is the formation of a tribromide, the dissociation constant of which is about 0·05.

CEYLON MEDICAL COLLEGE,  
COLOMBO.

### XXXV.—*The Condensation of Aromatic Aldehydes with Nitromethane.*

By FREDERIC GEORGE PERCY REMFRY.

In the course of some experiments on the condensation of nitromethane with aromatic aldehydes by means of alcoholic potassium hydroxide, it was found that the facility with which condensation took place was greatly affected by the character as well as the position of substituting groups in the benzene nucleus. An indication that such would be the case was given by the results obtained by previous investigators. Thus Posner (*Ber.*, 1898, **31**, 656), using zinc chloride as condensing agent, was able to prepare  $\omega$ -nitrostyrenes from *o*- and *m*-nitrobenzaldehyde, but not from the para-compound or other substituted benzaldehydes even when using different condensing agents. On the other hand, Thiele (*Ber.*, 1899, **32**, 1293), by the use of alcoholic potassium hydroxide, was able to obtain, apparently in each case with equal ease, *o*-*o*, *o*-*m*, and *o*-*p*-dinitrostyrene. It was deemed of interest to make an extended study of the condensation products of nitromethane with various substituted benzaldehydes with the view of ascertaining, so far as possible, the conditions which govern this reaction. A large number of aromatic aldehydes were therefore treated with nitromethane in the presence of alcoholic potassium hydroxide under exactly similar conditions. The results obtained, however, do not admit of any generalisation with regard to the condensation of aromatic aldehydes with nitromethane, but have given some

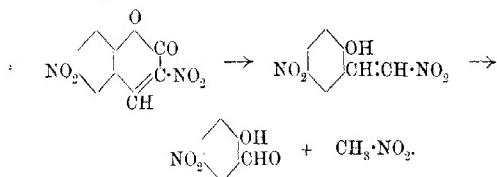
indication of the effect of certain groups in various positions; anomalies have, however, been observed.

Commencing with monosubstituted benzaldehydes, it was found that the hydroxyl groups in the ortho- or meta-position exerted no influence on the course of the reaction, but that a para-hydroxyl group, either alone or in conjunction with other groups (except in one instance), rendered condensation impossible. If, however, the para-hydroxyl group is closed by such means as methylating (Rosemund, *Ber.*, 1909, **42**, 4780), acetylating, or benzoylating, then condensation readily occurs. A free carboxy-group in the molecule prevents condensation, as is seen in the cases of *m*- and *aldehydophenoxyacetic acids*, but the esters of these two acids behave quite differently, and readily form nitrostyrenes. *p*-Chlorobenzaldehyde, on the other hand, readily condenses with nitromethane. Thiele (*loc. cit.*) has already shown that the presence of single nitro-group in any position in the ring (*o*-, *m*-, or *p*-, with regard to the aldehyde group) has no effect on the condensation, but, as will be proved later, the same cannot be said of the nitro-group when other substituents, which by themselves have no influence on the course of the reaction, are introduced as well. Both 3-nitro-4-methoxybenzaldehyde and 3:5-dinitro-4-methoxybenzaldehyde, where one and two nitro-groups respectively have been introduced into *p*-methoxybenzaldehyde, show a readiness to form nitrostyrenes about equal to that of the parent substance. *p*-Nitro-4-hydroxybenzaldehyde, however, having a free *p*-hydroxyl group, follows the hydroxyl rule, and does not condense.

The one apparent exception to this rule is found in 5-aldehydosalicyclic acid, which readily combines with nitromethane. This exceptional reaction may be explained by the supposition that in solution a lactone is formed, and hence no free *p*-hydroxyl group is really present. In support of this theory, it was found that if the carboxylic acid was esterified, no condensation took place, the formation of a lactone being then impossible, and the *p*-hydroxyl group being thus free to exercise its obstructive effect. Similarly, 3-aldehydosalicyclic acid may be considered to form a lactone, seeing that condensation takes place; on esterification, however, no condensation occurs. This was certainly unexpected, seeing that a free *o*-hydroxy group alone does not hinder condensation, and all cases in which a carboxylic ester has been the only substituent in the molecule have proved amenable to condensation.

The addition of a nitro-group to either of these aldehydo-acids prevents condensation, presumably by hindering the closing of the lactone ring. When two hydroxy-groups are present in the ortho- and meta-position, the aldehyde acts normally, that is, as if only

one were present at a time, and condensation readily takes place. When, however, one of the hydroxy-groups is in the para-position, no styrene is formed. This was found on trying to condense the carbonate of 3:4-dihydroxybenzaldehyde with nitromethane, potassium hydroxide at once liberating the hydroxy-groups, and a quantitative yield of protocatechualdehyde being obtained. When the hydroxy-groups are bound, however, as in 3:4-methylenedioxybenzaldehyde, condensation readily takes place, as would be expected. While experimenting with nitrosalicylaldehydes, it was found that the position of the nitro-groups was of importance, for whereas 3-nitrosalicylaldehyde undoubtedly formed a nitrostyrene, although in small quantities, the 5-nitro-compound did not. Additional evidence of the fact that 5-nitrosalicylaldehyde does not condense in the usual way with nitromethane is furnished by Clayton (Trans., 1910, **97**, 1390), who obtained nitrostyrenes by the action of alkalis on certain derivatives of coumarin. In the case of 3:6-dinitrocoumarin, however, the reaction proceeded in the following manner:



In order to account for the production of 5-nitrosalicylaldehyde, the intermediate formation of  $\omega$ -5-dinitro-2-hydroxystyrene must be supposed, but no trace of it could actually be isolated. This evidence cannot, however, be taken as strong proof that 5-nitrosalicylaldehyde will not under any conditions condense with nitromethane to form the desired nitrostyrene, seeing that Clayton treated the different coumarins with boiling aqueous alkali hydroxide or ammonia, whilst in the experiments described in this paper, temperatures below  $0^{\circ}$  were employed, and even then in some cases only a very small quantity of condensation product was obtained. It may, however, be assumed from Clayton's work that the presence of an alkyl group in any position round the ring has no effect whatever on the course of the reaction with nitromethane. Moreover, it has been found that 1-aldehydo- $\beta$ -naphthol condenses just as readily as salicylaldehyde.

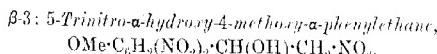
#### EXPERIMENTAL.

In all the experiments described in this paper, the method of procedure was practically identical, and, except in the matter of temperature, was similar to the method described by Rosenmund

(*Ber.*, 1909, **42**, 4780), Thiele, however, being the first to make use of alcoholic potassium hydroxide as a condensing agent in this reaction (*Ber.*, 1899, **32**, 1294), whereby he prepared styrenes from *o*-, *m*-, and *p*-nitrobenzaldehyde and terephthalaldehyde. A short account of the process in the first experiment will therefore serve for all.

One molecular quantity of the aldehyde was dissolved in sufficient absolute alcohol to prevent it crystallising out when the temperature of the solution was lowered to about  $-5^{\circ}$  by a freezing mixture. To this was added one and a-quarter molecular quantities of nitromethane. (Where a carboxyl or hydroxyl group is present in the molecule of the particular aldehyde to be condensed with nitromethane, one molecule of potassium hydroxide is added to neutralise it and one to effect the condensation.) Two molecular proportions of 50 per cent. potassium hydroxide, dissolved in about ten volumes of absolute alcohol, after being cooled below  $0^{\circ}$ , were slowly dropped from a tap funnel into the solution of the aldehyde, which was kept well stirred, and the temperature was not allowed to rise above  $0^{\circ}$ . As soon as all the alkali had been introduced, the alcoholic solution was diluted with an equal volume of water and rendered just acid by the addition of dilute hydrochloric acid. In many cases the required nitrostyrene crystallised direct from this solution, and was collected, washed with water, and recrystallised. If crystallisation did not take place, the excess of alcohol was removed, and the condensation product, as a rule, quickly separated from the aqueous liquor. Failing this, extraction with ether was resorted to.

For the sake of brevity and clearness, the compounds have been arranged in tabular form (p. 286), no detailed description of each substance being necessary, except in a few cases, owing to the similarity of their properties and methods of preparation. Except where mentioned otherwise, the colour of these compounds is of varying shades of yellow. All those aldehydes which were found to condense with nitromethane to form nitrostyrenes have been placed in table I, whilst those which did not are to be found in table II.



This substance was obtained when attempting to prepare  $\alpha$ -3: 5-trinitro-4-methoxystyrene. The results of the analyses show that water had not split off to form the expected styrene:

0·1310 gave 0·1840 CO<sub>2</sub> and 0·0371 H<sub>2</sub>O. C=38·3; H=3·17.  
 0·1524 " 0·2138 CO<sub>2</sub> " 0·0447 H<sub>2</sub>O. C=38·3; H=3·3.

TABLE I.

Compound.	Formula.	Crystalline form.	M. p.	Analysis.	
				Found, per cent.	Theory, per cent.
$\alpha$ -Nitro- $\alpha$ -hydroxystyrene .....	$\text{OHC} \cdot \text{CH}_2 \cdot \text{CH}(\text{OH}) \cdot \text{CH}_2 \cdot \text{NO}_2$	Prismatic needles	133-134°	N = 8.7	N = 8.5
$\alpha$ -Nitro- $\alpha$ -hydroxystyrene .....	$\text{OHC} \cdot \text{CH}_2 \cdot \text{CH}(\text{OH}) \cdot \text{CH}_2 \cdot \text{NO}_2$	"	132-133°	N = 8.6	N = 8.5
$\alpha$ -Nitro- $\alpha$ -hydroxystyrene* .....	$\text{OHC} \cdot \text{CH}_2 \cdot \text{CH}(\text{OH}) \cdot \text{CH}_2 \cdot \text{NO}_2$	Plat. needles	165°	N = 7.1	N = 6.8
$\alpha$ -Nitro- $\alpha$ -acetoxystyrene .....	$\text{CH}_3 \cdot \text{CO}_2 \cdot \text{CH}_2 \cdot \text{CH}(\text{OH}) \cdot \text{CH}_2 \cdot \text{NO}_2$	Silky needles	158-159°	N = 5.3	N = 5.2
Ethyl $\alpha$ -nitrostyryl- $\beta$ -oxoacetate .....	$\text{C}_2\text{H}_5 \cdot \text{CO}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{CH}_2 \cdot \text{CH}(\text{OH})_2 \cdot \text{CO}_2 \cdot \text{Et}$	Needle aggregates	82°	N = 5.6	N = 5.6
Ethyl $\alpha$ -nitrostyryl- $\beta$ -oxoacetate .....	$\text{NO}_2 \cdot \text{CH} \cdot \text{CH}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{CH}_2 \cdot \text{CO}_2 \cdot \text{Et}$	Needles	147-148°	N = 5.8	N = 5.6
<i>p</i> -Chloro- $\alpha$ -nitrostyrene .....	$\text{OHC} \cdot \text{CH}_2 \cdot \text{CH}(\text{NO}_2) \cdot \text{CH}_2 \cdot \text{NO}_2$	"	111-112°	N = 7.4	N = 7.3
$\omega$ -3-Dinitro-2-hydroxystyrene .....	$\text{OHC} \cdot \text{CH}_2 \cdot (\text{NO}_2)_2 \cdot \text{CH}_2 \cdot \text{CH}(\text{OH})_2 \cdot \text{NO}_2$	"	174-175°	N = 13.9	N = 13.3
$\omega$ -3-Dinitro-4-methoxystyrene .....	$\text{OMe} \cdot \text{C}_6\text{H}_3(\text{NO}_2)_2 \cdot \text{CH}_2 \cdot \text{CH}(\text{NO}_2)_2$	"	165-166°	N = 12.7	N = 12.5
Ethyl 3-aldehydosalicylate .....	$\text{CHO} \cdot \text{C}_6\text{H}_4(\text{OH}) \cdot \text{CO}_2 \cdot \text{Et}$	Colorless needles	66-67°	{ C = 61.5 (H = 5.2)	C = 61.5 H = 5.1
Phenylhydrazone of 3-aldehydosalicylic acid .....	$\text{C}_6\text{H}_5 \cdot \text{NH}_2 \cdot \text{O}_2 \cdot \text{N}_2$	Amber prisms	188°	N = 11.0	N = 10.9
$\alpha$ -Nitro-2-hydroxy-3-ethoxy-styrene .....	$\text{OHC} \cdot \text{C}_6\text{H}_4 \cdot \text{CO}_2 \cdot \text{CH}_2 \cdot \text{CH}(\text{OH})_2 \cdot \text{NO}_2$	Needles	231°	N = 6.5	N = 6.7
5-Nitro-3-aldehydosalicylic acid † .....	$\text{C}_6\text{H}_3(\text{NO}_2)_2 \cdot \text{NH}_2 \cdot \text{O}_2 \cdot \text{N}$	Colorless needles	195-196°	N = 6.9	N = 6.6
Ethy 5-aldehydosalicylate .....	$\text{CH}_3 \cdot \text{C}_6\text{H}_3(\text{OH})_2 \cdot \text{CO}_2 \cdot \text{Et}$	Colorless prisms	69°	{ C = 61.8 (H = 5.3)	C = 61.8 H = 5.1
Phenylhydrazone of ethyl 5-aldehydosalicylate .....	$\text{C}_6\text{H}_5 \cdot \text{NH}_2 \cdot \text{O}_2 \cdot \text{N}_2$	Prisms	135-136°	—	—
Phenylhydrazone of 5-aldehydosalicylic acid .....	$\text{C}_6\text{H}_5 \cdot \text{NH}_2 \cdot \text{O}_2 \cdot \text{N}_2$	Prismatic needles	219°	N = 11.1	N = 10.9
Ethy 3-nitro-5-aldehydosalicylate .....	$\text{C}_6\text{H}_3(\text{NO}_2)_2 \cdot \text{NH}_2 \cdot \text{O}_2 \cdot \text{N}$	Colorless needles	79-80°	N = 6.0	N = 5.8
1,6-Nitrovinyl- $\beta$ -naphthoate .....	$\text{OHC} \cdot \text{C}_6\text{H}_3(\text{NO}_2)_2 \cdot \text{CH}_2 \cdot \text{CH}(\text{NO}_2)_2 + 2\text{H}_2\text{O}$	Red needles	187-188°	N = 5.5	N = 5.6

\* Obtained by saponification of the acetyl derivative in weak alkalic hydrochloric acid solution.

† Prepared in the same way as 3-nitro-5-aldehydosalicylic acid.

0·1278 gave 15·7 c.c. N<sub>2</sub> at 24° and 770 mm. N = 14·4.

C<sub>9</sub>H<sub>9</sub>O<sub>8</sub>N<sub>3</sub> requires C = 37·6; H = 3·14; N = 14·6 per cent.

(C<sub>9</sub>H<sub>9</sub>O<sub>8</sub>N<sub>3</sub> " C = 40·1; H = 2·6; N = 15·6 " )

Moreover, this substance is readily soluble in dilute alkali hydroxides, whereas nitrostyrenes are almost insoluble.

### 3-Nitro-5-aldehydosalicylic Acid.

5-Aldehydosalicylic acid is dropped in small portions into a mixture of a little more than the theoretical quantity of nitric acid (D 1·142) and twelve times its weight of concentrated sulphuric acid kept at a temperature of between -5° and -10° by a freezing mixture. After remaining at the ordinary temperature for two hours, the solution is poured on to ice, the resulting solid collected, washed with a little ice-water, and crystallised from hot water. Fine yellow needles are obtained, which give off water of crystallisation rapidly at 110°, and melt at 177°. For analysis, the substance was dried at 100°:

0·1543 gave 9·4 c.c. N<sub>2</sub> at 21° and 771 mm. N = 7·2.

C<sub>8</sub>H<sub>7</sub>O<sub>6</sub>N requires N = 6·6 per cent.

0·5866 lost 0·0450 H<sub>2</sub>O at 110°. H<sub>2</sub>O = 7·67.

C<sub>8</sub>H<sub>7</sub>O<sub>6</sub>N.H<sub>2</sub>O requires H<sub>2</sub>O = 7·42 per cent.

### $\beta$ -Nitro-a-2:5-trihydroxyphenylethane.

As nothing crystalline separated from the reaction mixture, this was extracted with ether, the ether dried and evaporated, when a dark oil was left. After long keeping in an evacuated desiccator, the oil gradually crystallised. The crystals were freed from adherent oil by pressing on porous plate, and dissolved in dilute alcohol, from which large, prismatic needles of a ruby colour crystallised out. On drying in the air, the colour changed to a brick red, and the crystals then melted at 182°. For analysis, they were dried, first at 100°, then at 110°:

0·1272 gave 7·7 c.c. N<sub>2</sub> at 22° and 757 mm. N = 7·0.

C<sub>8</sub>H<sub>9</sub>O<sub>5</sub>N requires N = 7·0 per cent.

The styrene of the above contains 7·7 per cent. of nitrogen, and from the result of the analysis it was evident that the above alcohol had been obtained instead.

### Condensation Product of Nitromethane and 5-Nitrosalicylaldehyde.

After having removed some of the alcohol which served as solvent during the condensation, the first crop of crystals proved to be unchanged 5-nitrosalicylaldehyde. Subsequent crops were found to be mixtures, and, to effect a separation, they were each

in turn dissolved in ether, the solution shaken with a concentrated solution of sodium hydrogen sulphite to remove unchanged aldehyde, then once with water, and afterwards dried over calcium chloride. On evaporating off the ether, an almost colourless substance remained. This was crystallised from glacial acetic acid, from which were obtained pale straw-coloured, needle-shaped crystals, melting at 237–238°. The yield was very small. After drying in an evacuated desiccator, the substance was analysed.

0·1320 gave 17·2 c.c. N<sub>2</sub> at 21° and 770 mm. N=15·4.

0·1234 .. 16·2 c.c. N<sub>2</sub> .. 22° .. 765 mm. N=15·4.

0·1268 .. 0·2154 CO<sub>2</sub> and 0·0382 H<sub>2</sub>O. C=46·3; H=3·43

C<sub>7</sub>H<sub>6</sub>O<sub>4</sub>N<sub>2</sub> requires C=46·1; H=3·2; N=15·4 per cent.

(C<sub>8</sub>H<sub>6</sub>O<sub>5</sub>N<sub>2</sub>) .. C=45·7; H=2·9; N=13·3 ..

The results of the analyses prove that the substance obtained was not the expected *ω*-dinitro-2-hydroxystyrene, but a compound having the empirical formula C<sub>7</sub>H<sub>6</sub>O<sub>4</sub>N<sub>2</sub>.

TABLE II.

*Aldehydes which will not Condense with Nitromethane.*

<i>p</i> -Hydroxybenzaldehyde.	5-Nitro-3-aldehydosalicilic acid.
<i>p</i> -Aldehydophenoxyacetic acid.	Ethyl 5-aldehydosalicylate.
<i>m</i> -Aldehydophenoxyacetic acid.	3-Nitro-5-aldehydosalicilic acid.
3-Nitro-4-hydroxybenzaldehyde.	Ethyl 3-nitro-5-aldehydosalicylate.
Ethyl 3-aldehydosalicilate.	Protoproctechnaldehyde.

THE WELLCOME CHEMICAL WORKS,  
DARTFORD, KENT.

XXXVI.—*The Interaction of Alloxan and Glycine.*

By WILLIAM HOLDSWORTH HURTLEY and WILLIAM ORD WOOTTON

STRECKER (*Annalen*, 1862, **123**, 363) was the first to examine the action of alloxan on amino-acids. He found that on warming a solution of alloxan with a solution of leucine, *isovaleraldehyde* and carbon dioxide were produced, and that alanine, when treated in the same way, gave acetaldehyde and carbon dioxide, whilst glycine gave no aldehyde,<sup>a</sup> but did give carbon dioxide; in all three cases the liquid assumed the colour of murexide. No quantities were given in Strecker's paper, and he identified his products by qualitative tests only.

Piloty and Finkl (*Annalen*, 1901, **333**, 22), in their paper<sup>b</sup>

<sup>a</sup> Formaldehyde was first obtained by Hofmann in 1867.

FIG. 1.

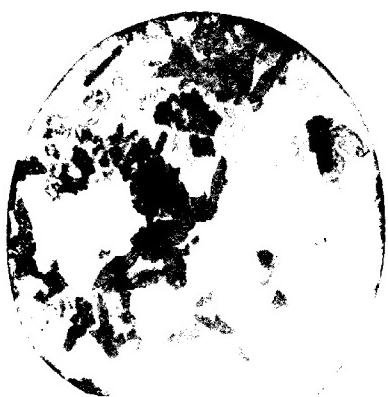


FIG. 2.



Figs. 2 to 7 show the several stages of the reaction as it occurs in moderately dilute solution.

FIG. 3.

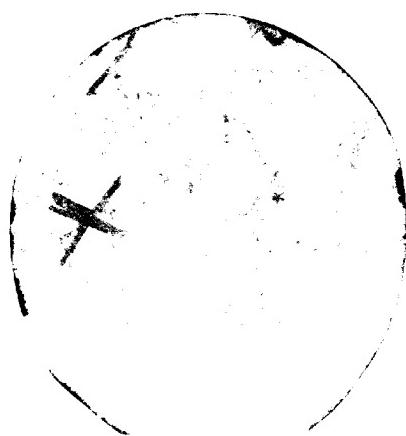


FIG. 4.



FIG. 5.

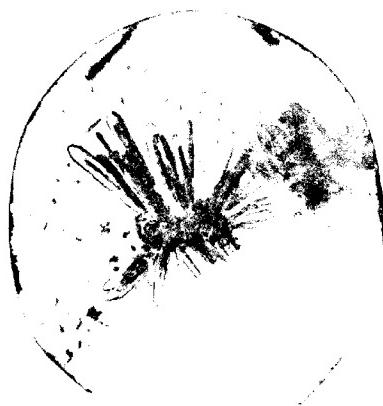


FIG. 6.

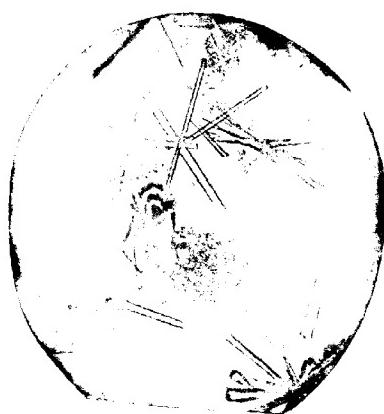


FIG. 7.

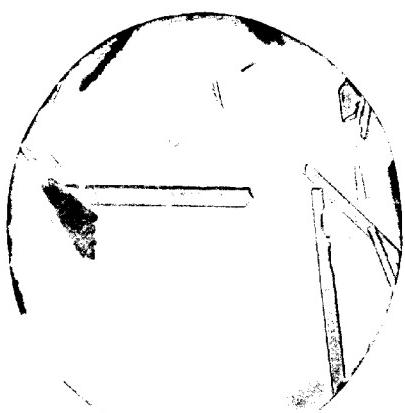


FIG. 8.



( $T_{\text{sat}} = -25$ )

the constitution of murexide, describe the interaction of alloxan and glycine when concentrated solutions are mixed at 80°. In these circumstances, the colour of murexide is produced, carbon dioxide is evolved, and, on rapidly cooling, a crystalline product is obtained which has the colour of murexide; this product they describe as glycine purpure. When, instead of cooling the mixture, it was heated until the colour of the murexide had disappeared, an insoluble, amorphous substance was deposited, and the mother liquor yielded a yellow, crystalline solid, which they describe as uramiloacetic acid:



Piloty and Finkh make no reference to the production of formaldehyde.

The apparently abnormal behaviour of glycine towards alloxan led us to repeat the earlier experiments. In the first place, we confirmed the production of *isovaleraldehyde* from leucine and of acetaldehydes from alanine by preparing the *p*-nitrophenylhydrazone of these aldehydes; we also tried the action of alloxan on  $\alpha$ -amino-butyric acid, and were able to show that propaldehyde was produced, which we confirmed by an analysis of the *p*-nitrophenylhydrazone.

When molecular proportions of alloxan and glycine were heated in concentrated solution, no formaldehyde was produced, but we obtained the amorphous substance and the uramiloacetic acid of Piloty and Finkh. When solutions of glycine and alloxan were heated under the exact conditions stated by Piloty and Finkh, we obtained the product they describe as glycine purpure, also the amorphous substance, and the compound they describe as uramiloacetic acid. Under these conditions, no formaldehyde appears to be liberated. Our analytical results for the glycine purpure approximate to those of Piloty and Finkh:

P. and F.	H. and W.
N = 23.89 (dried at 115°)	24.17 (air-dried).
N = 21.46 " "	22.47 (dried at 115°).

On examining the substance under a high power of the microscope, however, it appeared to be far from homogeneous. Fig. 1 shows a typical preparation. It will be seen to contain (*a*) torpedo-shaped crystals, brown by transmitted and green by reflected light; (*b*) pink, rectangular crystals, showing light crosses; (*c*) red, amorphous matter. We prepared the substance six times, always with the like result, and we cannot believe that Piloty and Finkh's glycine purpure is a definite substance.

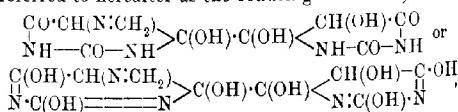
When molecular proportions of alloxan and glycine in dilute solution are distilled, formaldehyde is easily recognised in the

distillate, the yield being about 7·5 per cent. of the theoretical. This low yield of formaldehyde is accounted for below. Under these conditions, Piloty and Finkh's amorphous substance is not obtained. The liquid, which becomes purple soon after mixing, loses its purple colour and turns yellow, crystals of a substance closely related to uramil (the torpedo-shaped crystals referred to above) being deposited. The filtrate from these deposits crystallises apparently identical with Piloty and Finkh's uramiloacetic acid. If the acid mother liquor from the product is evaporated, a red, gummy substance is obtained which does not contain oxalic acid, but if the liquor is neutralised with ammonia and then evaporated crystals of ammonium oxalate are deposited in considerable quantity.

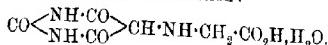
The reaction between these substances evidently occurs at moderate dilutions in several distinct stages. To a certain extent the course of the reaction can be followed by removing drops of the solution at intervals and allowing them to crystallise on a microscope slide. Under these conditions the first substance to appear is murexide, which separates in typical, prismatic crystals (Fig. 2). This is formed even at the ordinary temperature, and its presence is sufficient to account for the purple colour rapidly assumed by the mixed solutions. On warming, the colour of murexide rapidly vanishes, with evolution of carbon dioxide, but at 20° it persists for some time, and in both cases crystals of another substance, distinct from murexide, make their appearance. These are shown in Figs. 3 and 4. This compound is closely allied to uramil, and is readily converted into this substance by repeatedly dissolving it in aqueous sodium hydroxide and precipitating it by hydrochloric acid. On analysis, it gives figures agreeing well with the formula:



On continuing to heat the liquid, it turns yellow, and, on boiling, formaldehyde is evolved. At this stage another substance is produced, namely, the uramiloacetic acid of Piloty and Finkh (Figs. 5, 6, and 7). The results of our analyses of this well-defined compound agree with those of Piloty and Finkh, but we arrive at the formula  $\text{C}_9\text{H}_{11}\text{O}_7\text{N}_5$ , whereas Piloty and Finkh assign to it the formula  $\text{C}_8\text{H}_9\text{O}_4\text{N}_3$ . We believe it to be 2: 4: 6: 2': 4': 5': 6'-hepto-hydroxy-5-methylcneamino-4: 5: 4': 5'-tetrahydro-4: 4'-dipyrimidyl. (It is referred to hereafter as the reducing substance.)

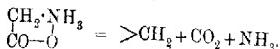


Piloty and Finkh give it the constitution :



Our constitutional formula is based on the following reactions of the substance : (1) When hydrolysed by boiling with water, dilute sulphuric acid or sodium hydroxide, it gives formaldehyde. (2) It has powerful reducing properties ; thus, on adding a solution to a dilute solution of silver nitrate or to a dilute solution of gold chloride, it gives in each case a colloidal solution of the metal. (3) Ammonia converts it into an exceedingly insoluble amide. (4) When treated with moderately dilute nitric acid, it gives alloxan and evolves formaldehyde. (5) It is a distinctly acidic substance.

The course of the reaction appears to be as follows : The glycine loses ammonia and carbon dioxide :



whilst the methylene group thus liberated reduces a part of the alloxan to dialuric acid, and is itself converted for the most part into formaldehyde. The unchanged alloxan and the dialuric acid form alloxantin, which, with the ammonia, forms murexide. Direct proof that the liquid contains alloxantin has been obtained. In the acid solution the murexide is transformed into the substance we have described as being closely related to uramil, and this product, or the uramil derived from it, condenses with dialuric acid and formaldehyde to give the reducing substance.

The final gummy product of the reaction has not yet been fully investigated, but from the fact that it readily gives a large yield of ammonium oxalate, it is clearly a product or mixture of products resulting from the opening of the pyrimidine ring.

We have shown that dimethylalloxan also oxidises an  $\alpha$ -amino-acid to the next lower aldehyde, and yields tetramethylmurexide. From this it appears certain that in the oxidation of an amino-acid by alloxan, the imino-groups of the latter are not involved.

In addition to the amino-acids mentioned before, we have tried the action of alloxan on tyrosine, tryptophan, cystine, and on glucosamine ; all these give a strong murexide colour, and in the case of tyrosine a flowery odour is produced. That alloxan deeply colours the skin has long been known ; this action is mentioned by Liebig and Wöhler ; we have tried its action on peptone (Witte's), gelatin, and casein. It gives a feeble murexide colour on warming with the first two, but no colour with the third. These results seem to show that alloxan might be of some service in the classification of the proteins. As another matter of biochemical interest we may recall an observation of Liebig to the effect that he found

free alloxan in the jelly-like mucus obtained from a case of intestinal catarrh. The ease with which considerable quantities of ammonium oxalate are formed by the interaction of alloxan and glycine is also of interest when it is remembered that there is some difficulty in accounting for the endogenous oxalates of the urine. Lastly, if the interaction of alloxan and glucosamine follows the normal course, a pentose should be formed from the glucosamine.

The reaction promises to be one of considerable biochemical interest, and is being further studied from this point of view. One of the products described in this paper is being examined as to its physiological action.

#### EXPERIMENTAL.

##### *Action of Alloxan on $\alpha$ -Aminobutyric Acid.*

Twenty-four grams of alloxan dissolved in 50 c.c. of warm water were added to a solution of 10 grams of  $\alpha$ -aminobutyric acid in 25 c.c. of warm water. The solution almost immediately became purple-red, and, on heating, a brisk evolution of carbon dioxide occurred, and crystals of murexide separated. On distillation the liquid became dull red, and a micro-crystalline deposit formed whilst an odour of propaldehyde became perceptible. The distillate reduced ammoniacal silver nitrate, gave a resin with sodium hydroxide, and on treatment with *p*-nitrophenylhydrazine gave a yellow, crystalline hydrazone, melting at 120–121°. (Found. N = 22·00. Calc., N = 21·76 per cent.)

The yield of aldehyde in this reaction is illustrated by the following figures: 2·2 grams of alloxan and 1·0 gram of  $\alpha$ -aminobutyric acid gave 0·67 gram of the *p*-nitrophenylhydrazone; theory requires 1·87 grams. Yield, 35·8 per cent. By using twice the above quantity of alloxan, the yield of hydrazone was raised to 52·4 per cent.

##### *Action of Alloxan on Glycine.*

A. *In Concentrated Solutions.* 2·9 Grams of alloxan (1 mol.) and 1 gram of glycine (1 mol.) in 20 c.c. of water rapidly gave a deep purple liquid, and deposited a purple solid. The liquid, after boiling for twenty minutes, gave 0·6 gram of a brick-red solid. The filtrate from this was brownish-yellow, and slowly deposited 0·5 gram of orange crystals. The mother liquor from these, when treated with alcohol, gave a yellow, amorphous precipitate (0·5 gram), and the mother liquor from this precipitate turned red when allowed to remain in the air, and on evaporation deposited a brownish-red, amorphous substance, which was not examined. The brick-red solid was mostly uramil, but contained a yellow substance

sparingly soluble in alkalis, which, on oxidation with bromine water and sodium hydroxide, gave an intense blue fluorescence recalling that observed by Hartley (Trans., 1905, **87**, 1791) in the preparation of murexide from alloxanthin by the action of ammonia on it. The orange crystals were identical with a product which is fully described later. The yellow, amorphous substance evolved ammonia freely when boiled with sodium hydroxide; it does not appear to contain the alloxan ring.

B. *In Dilute Solution*.—A solution of 3·5 grams of glycine and one of 10 grams of alloxan (molecular proportions) were made up to 500 c.c. It gradually became deep purple on heating, and after ten minutes very small, silky crystals separated in great number. These crystals were torpedo-shaped, and with them was a small quantity of minute, needle-shaped crystals; the weight of this product was 1 gram. The filtrate, when evaporated to a smaller bulk on the water-bath, deposited 1·5 grams of yellow crystals. On further concentration, a red, gummy substance remained permeated with yellow crystals. When this gummy substance was allowed to remain in the air or in a vacuum desiccator, it swelled up, owing to a very slow and continuous disengagement of a gas; it was strongly acid, but contained no oxalic acid. On boiling with ammonia, however, it yielded ammonium oxalate. On treatment with nitric acid, it gave, amongst other products, crystals closely resembling those of carbamide nitrate. On boiling with sodium hydroxide, ammonia was evolved.

When this experiment was repeated exactly as above, except that after removal of the yellow crystals 45 c.c. of strong ammonia were added, a white precipitate of minute, felted needles (0·25 gram) was obtained, identical with the amide obtained from the yellow crystals which is referred to later. The filtrate from these, on evaporation, deposited 4·95 grams of ammonium oxalate in colourless, shining needles. (Found, N=17·92. Calc., N=17·50 per cent.)

Besides the substance referred to above, carbon dioxide and formaldehyde were given off when the solution was boiled. The former was estimated by making an experiment on 0·387 gram of glycine, working as above, and it gave 0·236 CO<sub>2</sub>, or 96·7 per cent. of the theoretical yield from the glycine; the latter was estimated by making an experiment on 0·511 gram of glycine, working as above, when 0·015 gram of formaldehyde was obtained, or 7·5 per cent. of the theoretical yield from the glycine. The remainder of the formaldehyde split off from the glycine is used up (*a*) in reducing alloxan, (*b*) in the production of the reducing substance.

As we have already pointed out, when glycine and alloxan are

allowed to react in hot concentrated solutions, the precipitate obtained, namely, Pilaty and Finkh's glycine purpurate, is not a homogeneous substance. When the reaction is performed in dilute solution, the murexide remains in solution, and rapidly undergoes further change. It was isolated as follows: 10 c.c. of a 10 per cent. glycine solution (1 mol.) were mixed with 12·4 c.c. of ammonia (1 mol.), and 20 c.c. of alloxan solution (2 mols.) were added. The mixture immediately became dark purple, and deposited red crystals with a green reflex (0·85 gram). The dried product was seen to consist of murexide-like prisms mixed with about an equal amount of a red powder; a drop of the liquid allowed to crystallise under the microscope deposited typical murexide crystals and spherical aggregates of exceedingly minute crystals (Fig. 8). These two products were separated by sieving through copper gauze of 10 mesh, and analysed:

0·0969 (prisms) gave N\* = 29·47.

0·1993 (spheres) gave N = 29·51.

$C_8H_8O_4N_6$  requires N = 29·58 per cent.

On repeating the last experiment, substituting an equivalent amount of sodium hydroxide for the ammonia, a deep purple liquid was obtained, which deposited a dull red precipitate, consisting of sodium hydrogen purpurate in the form of minute needles. (Found, N = 25·06; Na = 7·98. Calc., N = 24·22; Na = 7·96 per cent.)

The substance which immediately succeeds the murexide in the interaction of alloxan and glycine is best obtained by allowing the two substances to react in molecular proportions at the ordinary temperature in dilute solution. Thus, from 5 grams of alloxan, 1·8 grams of glycine, and 250 c.c. of water, a pale pink precipitate of silky, torpedo-shaped crystals appears after an hour:

0·2250 gave 0·2616  $CO_2$  and 0·0534  $H_2O$ . C = 32·56; H = 2·64; N = 27·66.

$C_8H_8O_4N_6$  requires C = 32·00; H = 2·67; N = 28·00 per cent.

Uramil,  $C_4H_4O_3N_3$  requires C = 33·57; H = 3·5; N = 29·37 per cent.

By dissolving in aqueous sodium hydroxide and reprecipitating by hydrochloric acid half a dozen times, this substance gave pure uramil. It is always formed when alloxan acts on glycine, and has always the same curious crystalline form. We think it is probably a definite substance of the above formula. The specimen of uramil obtained from it was analysed. (Found, C = 33·37; H = 3·45; N = 29·20. Calc., C = 33·57; H = 3·5; N = 29·37 per cent.)

The yellow crystals of the reducing substance, which we regard

\* Owing to the difficulty of obtaining the nitrogen free from nitric oxide in the ordinary method of combustion, the nitrogen was determined in all cases by Kjeldahl's method.

as the most important product of the reaction, are best obtained as follows: 10 grams of alloxan were dissolved in water and the solution made up to 500 c.c., 1·75 grams of glycine were added, and the whole heated to boiling during fifteen minutes, and then boiled briskly for half an hour. After twelve hours, 0·85 gram of crystals was collected. By concentrating the filtrate on the water-bath, successive crops of 0·4, 1·5, and 0·65 gram of the crystals (total, 3·4 grams) were obtained. The whole yield was crystallised from hot water, taking care to avoid prolonged boiling, which brings about hydrolysis. If in this preparation the volume is made up to 300 c.c. only, the crystals of reducing substance are mixed with the torpedo-shaped crystals described above, and the yield is diminished.

*2:4:6:2':4':5':6'-Heptahydroxy-5-methyleneamino-4:5:4':5'-tetrahydro-4:4'-dipyrimidyl* forms very pale yellow prisms with pointed ends, as shown in Fig. 7. It has no definite melting point, but becomes dark purple at 165°; at 250° it sinters, forming a white sublimate, and there is no melting below 300°. It is sparingly soluble in the usual organic solvents, but dissolves readily in warm water:

0·1829 gave 0·2228 CO<sub>2</sub> and 0·0645 H<sub>2</sub>O. C=33·20; H=3·91.

0·1803, " 0·2207 CO<sub>2</sub>, " 0·0610 H<sub>2</sub>O. C=33·38; H=3·79.

0·0652, by Kjeldahl's method, gave N=22·17.

0·2262, " " " N=21·79.

C<sub>9</sub>H<sub>11</sub>O<sub>7</sub>N<sub>3</sub>H<sub>2</sub>O requires C=33·85; H=4·07; N=21·94 per cent.

Piloty and Finkh found for this substance C=33·03; H=3·95; N=21·02. Their formula, C<sub>9</sub>H<sub>9</sub>O<sub>7</sub>N<sub>3</sub> requires C=32·88; H=4·11; N=19·18 per cent. A solution of the compound in water gives with hydrochloric acid a nearly white, crystalline precipitate; the crystals have the same form, and show all the reactions of the original substance, and contain the same amount of nitrogen—an analysis gave 22·29 per cent. On boiling with water or with dilute sulphuric acid, formaldehyde is evolved; an estimation of the aldehyde obtained in each case gave 50 per cent. of that required by the formula assigned to the compound. The substance is readily soluble in sodium hydroxide, and on boiling the solution formaldehyde and ammonia are evolved; this can only be the case if one or both of the rings are opened. Piloty and Finkh's observation that alloxan is produced when the substance is treated with dilute nitric acid was confirmed, but it was also found that much formaldehyde is obtained on warming. If the nitric acid is more concentrated, a beautiful cherry-red liquid is produced. The most remarkable property of the substance is its strong reducing action; thus it reduces Fehling's solution in the cold; it forms colloidal

silver slowly from a neutral solution of silver nitrate at the ordinary temperature; a dilute solution of gold chloride quickly yields a colloidal gold solution, which is brownish-red by reflected and blue by transmitted light. Mercuric chloride is reduced to mercurous chloride also in the cold. It is readily oxidised by potassium permanganate, and yields well-defined products when treated with bromine water and with a solution of iodine in potassium iodide; these substances are at present under investigation.

The aqueous solution, when treated with ammonia and boiled, gave a silky, white precipitate, the liquid turning pink. The precipitate consisted of very minute needles, and it appears to be an amide of the reducing substance:

0·1193 gave 0·1554 CO<sub>2</sub> and 0·0470 H<sub>2</sub>O. C = 36·12; H = 4·38.  
0·0633 .. N = 28·75.

C<sub>9</sub>H<sub>12</sub>O<sub>6</sub>N<sub>6</sub> requires C = 36·0; H = 4·0; N = 28·0 per cent.

CHEMICAL LABORATORY,  
ST. BARTHOLOMEW'S HOSPITAL, E.C.

### XXXVII.—*Different Methods of Applying the Grignard Reagents.*

By HAROLD DAVIES, A.I.C., and FREDERIC STANLEY KIPPING.

In all those very numerous reactions in which the magnesium alkyl or aryl compounds, discovered by Grignard, are employed for synthetical purposes, the preparation of an ethereal solution of the reagent seems to be generally regarded as a necessary preliminary operation. In most cases this is a very easy task, but the quantity of pure ether required is considerable, and, particularly in the case of some of the aryl halides, the secondary formation of hydrocarbons not only causes loss of material, but often also very great inconvenience in the isolation of the compound which is afterwards prepared.

In synthesising some of the alkyl derivatives of silicon recently described, these disadvantages were overcome entirely, or to a very great extent, by omitting the preliminary preparation of the magnesium compounds. Benzylethylsilicon dichloride, for example, was obtained by gradually adding benzyl chloride to ethylsilicon trichloride in the presence of magnesium and ether (Luff and Kipping, Trans., 1908, **93**, 2006), and the mono-, di-, and tri-benzyl derivatives of silicon tetrachloride were prepared in a similar

manner from benzyl chloride, magnesium, and an ethereal solution of the silicon compound (Martin and Kipping, *Trans.*, 1909, **95**, 306).

In order to ascertain whether this modification of the usual method could be advantageously applied in other cases, a few experiments have been made on the preparation of carbinols from aldehydes, ketones, and esters (Grignard, *Compt. rend.*, 1900, **130**, 1322). The results have shown that in these reactions, also, the preliminary preparation of the magnesium compound is unnecessary, and that a good yield of the desired product is obtained by gradually adding a mixture of the alkyl or aryl halogen compound with the aldehyde, ketone, or ester, to the theoretical quantity of magnesium, which is covered with a little ether. The only instance in which this modified method was found to fail was in the case of acetone; that the process is capable of very general application is shown by the fact that it may serve in the synthesis of compounds, not only of carbon and of silicon, but also of tin.

A direct comparison of the yields obtained by the two methods in a given preparation has not been instituted (except in the case of some silicon compounds, *loc. cit.*), and it may be that sometimes the one, sometimes the other, procedure will give the better results, according to the nature of the interacting substances. It seems, however, that unless such a comparison has been made in a particular case, there is no reason for abandoning the method originally employed by Barbier (*Compt. rend.*, 1899, **128**, 110) in favour of that which is now so generally or universally adopted. In some appropriate instances, in fact, the desired substance may be prepared with the aid of magnesium and the halogen derivative, even when the corresponding Grignard compound cannot be obtained; thus, as Jaworsky has recently shown (*Ber.*, 1909, **42**, 435), many unsaturated alcohols may be prepared by treating ketones with magnesium and allyl bromide or iodide in presence of ether, although magnesium allyl halides of the usual type are unknown.

It need hardly be added that no claim is here made for the discovery of the method which has been studied, but it is hoped that the publication of this note will save time and trouble to many who are working with the Grignard reagents.

#### EXPERIMENTAL.

In preparing the carbinols by the modified method, the formation of a very small quantity of the Grignard compound was first started in the flask containing the magnesium and anhydrous ether; a mixture consisting of the aldehyde, ketone, or ester with the halogen compound, and diluted with an equal volume of ether, was then

added gradually from a tap funnel, the mixture in the flask being vigorously stirred, and cooled if necessary. The products were isolated in the usual manner.

Most of the experiments concern the use of benzyl chloride, because the preparation of magnesium benzyl chloride is more troublesome than that of the majority of the Grignard reagents.

*Phenylethylicarbinol* was prepared from benzaldehyde and ethyl bromide. The reaction proceeded without difficulty, and no secondary or decomposition products appeared to be formed; almost the whole of the crude product distilled constantly at 131—132°/50 mm., leaving very little residue; the yield of the carbinol was nearly theoretical. During the distillation the formation of water was not observed, and even when distilled under 750 mm. pressure, the carbinol boiled constantly at 210—211° without decomposing.

*Benzylmethylethylicarbinol* was prepared from methyl ethyl ketone and benzyl chloride; only small quantities were used, but the yield seemed to be satisfactory. On distillation under 747 mm. pressure, the carbinol decomposed, giving off water, and boiling at 215—225°. It has been described by Konowaloff (*J. Russ. Phys. Chem. Soc.*, 1904, **36**, 228).

*Triethylicarbinol* was obtained from diethyl ketone and ethyl bromide. During the preparation, colourless crystals, doubtless the additive compound, separated on the sides of the flask. The crude product distilled at 130—140°/747 mm. without decomposing, and the yield was at least 60 per cent. of the theoretical. It is described as an oil boiling at 140—142° under atmospheric pressure.

*Benzylphenylmethylcarbinol* was prepared from magnesium ( $\frac{1}{4}$  atoms), benzyl chloride ( $\frac{1}{2}$  mols.), and acetophenone (1 mol.) in dry ethereal solution. A gentle reaction set in, and continued until all the metal had disappeared. After the ether had been removed, the additive compound was decomposed with water, and the product was distilled under 30 mm. pressure; it did not boil at a constant temperature, but passed over from 170° to 200°, and appeared to be a mixture of the carbinol and the unsaturated hydrocarbon ( $\alpha$ -methylstilbene) derived from it. After several redistillations, however, a large proportion of it solidified on being kept for some time, giving the desired carbinol, which was easily obtained in a pure condition by recrystallisation from light petroleum. The compound has been described by Hell (*Ber.*, 1904, **37**, 457).

*Benzylethylpropylcarbinol*,  $C_6H_5CH_2\cdot CH_2\cdot CEtPr\cdot OH$ , was prepared by the interaction of ethyl propyl ketone and benzyl chloride; the yield was only about 60 per cent. of the theoretical, since, besides the carbinol, a rather large proportion of the unsaturated hydro-

carbon, derived from the carbinol by loss of water, was obtained. The carbinol boils at  $186^{\circ}/90$  mm., and a sample of the pure compound gave, on analysis, the following results:

0·1824 gave 0·5442 CO<sub>2</sub> and 0·1729 H<sub>2</sub>O. C = 81·3; H = 10·5.  
C<sub>13</sub>H<sub>20</sub>O requires C = 81·2; H = 10·4 per cent.

Benzylidimethylcarbinol could not be obtained by treating magnesium with a mixture of acetone and benzyl chloride, for although acetone reacts vigorously with a prepared solution of a Grignard compound, the presence of the ketone seems to retard or prevent the formation of magnesium benzyl chloride. This preparation was attempted several times, using acetone which had been dried with calcium chloride during several days, and then distilled, and also samples which had been first treated with a small quantity of a solution of the Grignard compound and then decanted; only negative results were obtained. In other experiments the formation of the Grignard compound was first started by the addition of a little benzyl chloride, and then the mixture of acetone and benzyl chloride was added, drop by drop, to the magnesium, but the vigorous action which was in progress soon ceased after a small proportion of the acetone had been added, and could not be made to start again. In a similar manner, the addition of acetone to an ethereal solution of magnesium ethyl bromide, which is reacting vigorously with magnesium, soon brings the interaction to a standstill.

*Phenylidibenzylcarbinol* was prepared from ethyl benzoate (1 mol.) and benzyl chloride (2 mols.) in presence of magnesium, the reaction proceeding without difficulty. The product was distilled under diminished pressure, and the distillate readily solidified to a hard, pale yellow cake. On recrystallisation from light petroleum, the carbinol was obtained in colourless needles; the yield was 60 per cent. of the theoretical. The compound has been described by Klages (*Ber.*, 1904, **37**, 1456). An attempt was made to prepare phenyl ethyl ketone by adding a mixture of ethyl benzoate (1 mol.) and ethyl bromide (1 mol.) to magnesium, but the product appeared to be a mixture of unchanged ethyl benzoate and phenyldiethylcarbinol.

*Dibenzylethylcarbinol*, CEt(CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>OH, was prepared from ethyl propionate and benzyl chloride in presence of magnesium and ether. When the ingredients had been mixed, the solution was heated under a reflux condenser for a short time, the ether was distilled off, and the residue heated at  $100^{\circ}$  during about two hours. The product was isolated in the usual manner, and the yield was good:

## 300 DIFFERENT METHODS OF APPLYING THE GRIGNARD REAGENTS.

0·1717 gave 0·5337 CO<sub>2</sub> and 0·1308 H<sub>2</sub>O. C=84·8; H=8·5.

C<sub>17</sub>H<sub>20</sub>O requires C=85·0; H=8·3 per cent.

*Dibenzylethylecarbinol* is a colourless, viscous liquid, boiling at 193°/12 mm. When cooled in a freezing mixture, it becomes very viscous, but does not crystallise, and when boiled under atmospheric pressure it decomposes slowly with elimination of water.

*Diethylstannic Chloride*, SnEt<sub>2</sub>Cl<sub>2</sub>.

Stannic chloride (1 mol.) was treated with ethyl bromide (1 mol.) in presence of magnesium and ether under the usual conditions with the intention of obtaining a mono-alkyl derivative of tin, but a compound of this type seemed not to be formed, or was produced in small quantities only. The principal product was diethylstannic chloride, which has been described by Pfeiffer (*Ber.*, 1902, 35, 3306), and which was identified by its melting point as well as by analysis.

*α-Bromo-αα-dibenzylpropane*, CEtBr(CH<sub>2</sub>·C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>.

For a purpose outside the scope of this investigation, experiments were made on the preparation of *α*-bromo-*αα*-dibenzylpropane, and on the conversion of this compound into *γγ*-dibenzyl-*n*-hexane; as the former operation is successful only under particular conditions, the results are here recorded. Dibenzylethylecarbinol (15 grams) is dissolved in dry ether (80 c.c.), and phosphorus tribromide (35 grams) is added gradually to the solution; the mixture, which becomes warm, is kept at the ordinary temperature for about twenty-four hours, then boiled under a reflux condenser for about an hour; finally the ether is distilled, and the residue is heated at 100° for about two hours. The product, when cold, is poured on ice, the bromide is extracted with ether, and the extract is washed with sodium carbonate solution, which removes phosphorus compounds. From the crude preparation which is obtained by the evaporation of the ethereal solution, the pure bromide is easily isolated by crystallisation from light petroleum. The yield is at least 85 per cent. of the theoretical.

The combined bromine was estimated by boiling the sample with an alcoholic solution of silver nitrate:

0·2861 gave 0·1765 AgBr. Br=26·1.

C<sub>15</sub>H<sub>10</sub>Br requires Br=26·4 per cent.

*α-Bromo-αα-dibenzylpropane* forms large, colourless prisms, and melts at 58–59°. It rapidly loses hydrogen bromide when it is heated at about 115°, and it cannot be distilled even under 13 mm. pressure.

Many unsuccessful attempts were made to prepare  $\gamma\gamma$ -dibenzyl-*n*-hexane. The bromide was treated with magnesium propyl bromide, and also with propyl bromide and magnesium in presence of ether, but in both cases the qualitative and quantitative analysis of the product showed it to consist principally, if not entirely, of an unsaturated hydrocarbon. An ethereal solution of the bromide was also heated with propyl bromide and sodium, but only the propyl bromide was attacked, and the  $\alpha$ -bromo- $\alpha\alpha$ -dibenzylpropane was recovered unchanged.

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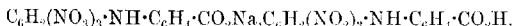
UNIVERSITY COLLEGE,  
NOTTINGHAM.

### XXXVIII.—*The Picraminobenzoic Acids and their Salts.*

By JAMES CODRINGTON CROCKER, M.A., D.Sc., and  
FRANK MATTHEWS, B.Sc.

SOME years ago, at the suggestion of Dr. G. S. Turpin, one of the authors examined the interaction of the three aminobenzoic acids and picryl chloride in the presence of alkali.

When *o*-aminobenzoic acid was treated in dilute alcoholic solution with the equivalent quantities of picryl chloride and sodium hydroxide, a scarlet, crystalline substance separated on cooling. On repeating the experiment in a solution containing less alcohol, golden-yellow crystals separated on cooling. Analysis showed the latter substance to be free from sodium, and the data agreed with the formula for *o*-picraminobenzoic acid. The scarlet crystals contained sodium, and the substance was shown to be an acid salt of the formula:



Similar results were obtained with *m*-aminobenzoic acid. In concentrated alcoholic solutions, the reaction gave a scarlet acid sodium salt, the analysis of which was in accordance with the above formula. In dilute alcoholic solutions, *m*-picraminobenzoic acid was formed, and separated as a fluffy, yellow mass. With *p*-aminobenzoic acid, only one product was obtained at the time. From concentrated alcoholic solutions, or solutions containing a moderate amount of water, the product of the reaction was *p*-picraminobenzoic acid, which separated in lustrous, yellow

leaflets. The ease with which these salts are hydrolysed is remarkable. Merely crystallising from dilute alcohol is sufficient to hydrolyse them completely to the acids, which separate in a pure state from the solution. The salt of *m*-picraminobenzoic acid is more easily hydrolysed than that of the corresponding ortho-acid. The salts can be crystallised from alcohol containing a little water, without change.

At this stage of the work a paper by Wedekind (*Ber.*, 1900, 33, 426) appeared, in which a brief account of the preparation and properties of the picraminobenzoic acids was given (*loc. cit.*, p. 431). The alkali salts were stated to crystallise well, and no further reference was made to them. The remarkable character of these salts appears to have been overlooked.

The work described above was discontinued for some time, and has been resumed recently. It has been found that the property of forming acid salts is characteristic of these three acids.

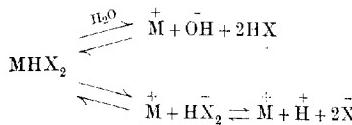
The authors have prepared acid salts of sodium, potassium, ammonium, methylamine, ethylamine, aniline, and pyridine, derived from the *o*-acid; and from the *m*-acid have obtained the corresponding salts of sodium, potassium, methylamine, ethylamine, and guanidine.

The acid salts of potassium and methylamine with the *p*-acid have also been prepared. Most of these acid salts show in a more or less marked degree the property of being hydrolysed by water. Even in the cold, when shaken with excess of water, the salts are gradually decomposed, with complete precipitation of the acid. These salts are not very soluble in water. On the other hand, some alkali salts of the normal type have been prepared, and they differ in character from the acid salts. They are readily soluble in water, and undergo very little hydrolysis even when boiled in aqueous solution. These salts are much more difficult to prepare than the acid salts. This property of forming acid salts would appear to be connected with the tendency of picryl derivatives to form additive compounds with substances the molecules of which contain nuclei of the benzene type. With this idea in view, the molecular weights of the acids were determined in acetone solution. The acids, however, were found to have simple unassociated molecules, so that the complex anions which give rise to the acid salts apparently do not exist to any extent in solutions of the acids. In the presence of a base, however, a normal salt would probably be first formed, and the residual affinity of this would be greater than that of the acid, and thus would favour the formation of the complex anion of the acid salt.

The remarkable behaviour of these salts in the presence of water

or dilute alcohol is to be ascribed mainly to the small solubility of the acids, and their very small affinity constants. The salts are thus easily attacked by water, and the acid is removed from the sphere of action by precipitation as soon as it is formed, so that in the presence of excess of water the hydrolysis proceeds to an end.

When the salt is shaken with water in quantity insufficient for complete hydrolysis, a state of equilibrium is eventually attained. In the solution the salt will probably dissociate electrolytically and hydrolytically, according to the scheme:



Let  $C_x$ ,  $C_i$ ,  $C_w$ ,  $C_a$ ,  $C_{oh}$  be the molecular or ionic concentrations respectively of the simple anion, the complex anion, water, the free acid, and hydroxyl, in the solution.

Also let  $C_x$  be the total ionic concentration of the cation of the salt in solution, and  $C_a$  the total concentration of the acid radicle in the combined and free state, in the solution. Then, if  $K_w$ ,  $K_a$ ,  $K$  are respectively the ionic product for water, the dissociation constant of the acid, and the "hydrolysis constant" of the salt, the state of equilibrium in the solution is defined by the following equations:

$$(1) \ C_a^2 C_{oh} = K C_i C_w.$$

$$(4) \ C_x + C_{oh} = C_{oh} + C_i + C_x.$$

$$(2) \ C_h C_{oh} = K_w.$$

$$(5) \ C_x = C_a + 2C_i + C_x.$$

$$(3) \ C_h C_x = K_a C_a.$$

These equations give the necessary data for finding the concentrations of the various ions and molecules in solution. It is clear at once from (1) that the concentration of the hydroxyl ions in solution should be constant whatever the quantity of salt originally taken, provided the water is not in excess. This fact was verified by a study of the hydrolysis of the acid potassium salt of the *o*-acid in water at 25°. When equilibrium was attained, the constant concentration of the free alkali was found to be  $4.36 \times 10^{-6}$  gram-equivalents per c.c. It follows from equation (2), also, that the concentration of the hydroniums is constant. Taking  $K_w$  to be  $1.2 \times 10^{-20}$  at 25°, this gave a value for  $C_h = 2.77 \times 10^{-15}$  gram-equivalents per c.c.

## EXPERIMENTAL.

*o-Picraminobenzoic Acid.*

For the preparation of this and the isomeric acids, equivalent quantities of picryl chloride (2·5 grams) and the amino-acid (1·4 grams) were separately dissolved in dilute alcohol (1:1), the hot solution mixed, and a dilute alcoholic solution of sodium hydroxide (0·8 gram) stirred into the mixture. On cooling, the picramino-derivative crystallised out. Wedekind's method of using two molecular proportions of amino-acid to one of picryl chloride involves the loss of one molecule of the former, this being converted into the hydrochloride.

*o-Picraminobenzoic acid* crystallises from alcohol in minute, acicular crystals of a golden-yellow tint, melting at 270° (Wedekind gives 271—272°), which are sparingly soluble in water, moderately so in boiling alcohol or acetone, and practically insoluble in ether. The yield of the substance was 2·2 grams. (Found, N=16·32. Calc., N=16·10 per cent.)

The solubility of the acid in water at 25° was determined:  
I. 65·80 grams of solution, saturated at 25° for six hours, gave 0·0244 gram of acid. Solubility=0·037 per 100 grams of solution.

II. 35·40 grams of solution, saturated at 25° for nine hours, gave 0·0175 gram of acid. Solubility=0·049 per 100 grams of solution.

Mean solubility=0·043 gram per 100 grams of solution.

In absolute alcohol at 50°, two experiments gave as the mean result, 0·482 gram per 100 c.c. of solution.

*m-Picraminobenzoic Acid.*

The yield of this acid, from the quantities given above, was 2·4 grams. On recrystallisation from dilute alcohol, minute, light yellow plates separated at first, but at a lower temperature a fluffy mass of fine needles was obtained. Both kinds of crystals melted sharply at 234° (Wedekind gives 233—234°). The substance is readily soluble in acetic acid or acetone, moderately so in methyl and ethyl alcohols, sparingly so in water, and insoluble in ether. (Found, N=16·03. Calc., N=16·10 per cent.)

The solubility in alcohol at 50° was determined. The mean result of two experiments was 1·200 grams per 100 c.c. of solution.

*p-Picraminobenzoic Acid.*

The yield of this acid, prepared as above, was 2·6 grams. The pure substance crystallises in pale yellow, spangled leaves, melting at 285° (Wedekind gives 292—293°).

It is sparingly soluble in alcohol or acetone, readily so in glacial acetic acid, and practically insoluble in water or ether. It is dissolved by alkalis to a deep red solution. (Found, N=16·13. Calc., N=16·10 per cent.)

The solubility in alcohol at 50° was determined. The mean of two experiments gave 0·220 gram per 100 c.c. of solution. The molecular weights of the three acids were determined in boiling acetone solution.

#### *Molecular Weights of the Picraminobenzoic Acids.*

w = weight of acid. Δ = elevation of boiling point.

V = volume of solution in c.c. M = molecular weight.

<i>o</i> -Acid.				<i>m</i> -Acid.				<i>p</i> -Acid.			
w.	V.	Δ.	M.	w.	V.	Δ.	M.	w.	V.	Δ.	M.
0·2568	12·5	0·54°	314	1·188	12·0	0·64°	343	0·4669	15·0	0·20°	346
"	21·0	0·30	337	"	14·0	0·55	343	"	22·0	0·15	314
"	23·5	0·27	334	"	15·5	0·50	341	"	30·5	0·10	340
Mean.....	328·3			"	17·0	0·46	338				
				Mean .....	341·2			Mean.....	338·3		

The calculated molecular weight for the simple unassociated molecule is in each case 348.

#### *Acid Sodium o-Picraminobenzoate.*

For the preparation of this salt, 2·5 grams of picryl chloride were dissolved in the least possible quantity of alcohol, and 1·4 grams of anthranilic acid in dilute alcohol (3:2). The solutions were mixed while hot, and a solution of 0·8 gram of sodium carbonate in dilute alcohol was rapidly stirred in. The colour of the solution became dark red, and on cooling slightly, minute, scarlet, needle-shaped crystals separated out. The yield was 2·2 grams. The substance was recrystallised from alcohol containing a little water. If dissolved in hot dilute alcohol (1:1), the acid separates, on cooling, in golden-yellow needles. The substance is slowly hydrolysed to the acid when in contact with cold water. The change is accelerated by shaking or heating. In the presence of excess of water, the change is complete, but, in general, some of the salt remains unchanged, and a state of equilibrium is set up between the salt, acid, and the base in solution. The substance is moderately soluble in water, but sparingly so in alcohol. It is rather more soluble in acetone than in alcohol, and is insoluble in benzene or ether. Excess of alkali easily dissolves the salt to a deep red solution, from which the acid is precipitated on addition of dilute acid. The salt decomposes gradually at 140°, the crystals becoming brown:

0·3201 gave 0·0290 Na<sub>2</sub>SO<sub>4</sub>. Na = 2·94.

0·4398 „ 0·0360 Na<sub>2</sub>SO<sub>4</sub>. Na = 2·65.

C<sub>26</sub>H<sub>12</sub>O<sub>6</sub>N<sub>8</sub>Na requires Na = 3·20 per cent.

The salt was also prepared from *o*-picraminobenzoic acid. 3·5 Grams of the acid were dissolved in boiling alcohol, and a solution of 0·3 gram of sodium hydroxide in alcohol containing a little water was stirred into it. A yield of 3 grams of the salt was obtained on cooling.

#### *Acid Potassium *o*-Picraminobenzoate.*

Four grams of *o*-picraminobenzoic acid were dissolved in boiling alcohol, and 3 c.c. (=0·6 gram KOH) of a 20 per cent. solution of potassium hydroxide in dilute alcohol (2:1) were stirred into the solution. The salt was precipitated immediately, and was washed with alcohol and ether. The yield was 3·5 grams. The substance consists of minute, glistening, scarlet crystals, which occur in elongated, six-sided plates. It is moderately soluble in water, and is hydrolysed by it slowly in the cold. On heating, the hydrolysis is rapid, and in presence of excess of water is complete, giving a yellow, powdery precipitate of the acid. It is sparingly soluble in alcohol, and is partly hydrolysed by the hot solvent. In acetone or methyl alcohol the substance is more soluble, but is again hydrolysed a little. It is insoluble in benzene or ether. With alkalis, deep red solutions are obtained, from which the acid is precipitated by dilute acids. As the salt explodes on heating directly with sulphuric acid, the analysis was effected by treating the salt first with hot water, and then with excess of dilute sulphuric acid to precipitate the acid. The filtrate from this was evaporated and the residue was ignited and weighed in the usual manner:

0·2546 gave 0·0300 K<sub>2</sub>SO<sub>4</sub>. K = 5·28.

0·5209 „ 0·0616 K<sub>2</sub>SO<sub>4</sub>. K = 5·30.

C<sub>26</sub>H<sub>12</sub>O<sub>6</sub>N<sub>8</sub>K requires K = 5·31 per cent.

The method of preparation and purification described above is typical for many of these salts, and except where otherwise stated is the method used.

#### *Acid Ammonium *o*-Picraminobenzoate.*

3·5 Grams of *o*-picraminobenzoic acid, treated with 0·12 gram of ammonia, gave 2·8 grams of the salt.

The substance consists of radiating clusters of scarlet needles. It is insoluble in ether, and sparingly soluble in ethyl and methyl alcohols, but readily so in water, and is hydrolysed partly to the acid in the cold. Even alcoholic solutions gave, on partial evaporation, a mixture of acid and salt. The salt can, however, be

crystallised unchanged from alcohol containing a very little ammonia. For the analysis, a weighed quantity was treated with hot water, and then the acid was precipitated by the addition of hydrochloric acid. After filtration, the solution was evaporated with platinum chloride, and the estimation was then completed in the usual manner:

0·3520 gave 0·0840  $(\text{NH}_4)_3\text{PtCl}_6$  and 0·0047 Pt.  $\text{NH}_4 = 2\cdot18$ .

0·4096 " 0·0980  $(\text{NH}_4)_3\text{PtCl}_6$  " 0·0012 Pt.  $\text{NH}_4 = 1\cdot99$ .

$\text{C}_{26}\text{H}_{19}\text{O}_{16}\text{N}_9$  requires  $\text{NH}_4 = 2\cdot52$  per cent.

#### *Silver o-Picraminobenzoate.*

1·75 Grams of the acid, treated with 0·9 gram of silver nitrate, gave 1 gram of the dark red salt. It is insoluble in water, alcohol, or ether. For analysis, the salt was decomposed by dilute sulphuric acid in excess. The precipitated acid was removed, and the silver was weighed as the sulphate:

0·2874 gave 0·0947  $\text{Ag}_2\text{SO}_4$ . Ag = 22·81.

0·2688 " 0·0891  $\text{Ag}_2\text{SO}_4$ . Ag = 22·95.

$\text{C}_{13}\text{H}_7\text{O}_5\text{N}_4\text{Ag}$  requires Ag = 23·68 per cent.

The salt is thus one of the normal series.

#### *Acid Methylammonium o-Picraminobenzoate.*

Three grams of the acid, treated in the usual manner with 0·2 grams of methylamine, gave 3 grams of the salt.

The substance consists of minute, yellowish-red needles, melting and decomposing at 234—235°. It is partly soluble in water, and is hydrolysed by it readily to the acid, which is precipitated as a yellow powder. It is sparingly soluble in methyl and ethyl alcohols, and is insoluble in benzene or ether.

With potassium hydroxide, a deep red solution is obtained, from which the methylamine is not evolved so readily as from an equivalent solution of methylamine hydrochloride:

0·1978 gave 29·9 c.c.  $\text{N}_2$  (moist) at 18·8° and 760 mm. N = 17·4.

0·9471 " 0·2556  $(\text{NH}_3\text{Me})_2\text{PtCl}_6$  and 0·0127 Pt.  $\text{NH}_3\text{Me} = 4\cdot02$ .

$\text{C}_{27}\text{H}_{21}\text{O}_{16}\text{N}_9$  requires N = 17·34;  $\text{NH}_3\text{Me} = 4\cdot26$  per cent.

#### *Acid Ethylammonium o-Picraminobenzoate.*

3·5 Grams of o-picraminobenzoic acid, treated in alcoholic solution with 9·34 gram of ethylamine, gave 2·5 grams of the salt.

The crystals are short, dark red prisms, crystallising in compact, radiating clusters. They melt and decompose at 24°, and are soluble in water, but are partly hydrolysed to the acid. Alkalies dissolve the salt to a deep red solution, but the ethylamine is not

liberated with the usual readiness on warming. In methyl and ethyl alcohols the substance is sparingly soluble, and if such solutions are partly evaporated, a mixture of acid and salt separates. The substance is readily soluble in acetone with partial decomposition, and is insoluble in ether. Dilute acids instantly precipitate the acid from a solution of the salt:

0·6418 gave 0·1700  $(\text{NH}_3\text{Et})_2\text{PtCl}_6$  and 0·0194 Pt.  $\text{NH}_2\text{Et} = 6\cdot23$ .  
 0·3689 " 0·1031  $(\text{NH}_3\text{Et})_2\text{PtCl}_6$  " 0·0053 Pt.  $\text{NH}_2\text{Et} = 5\cdot68$ .  
 $\text{C}_{28}\text{H}_{23}\text{O}_{16}\text{N}_9$  requires  $\text{NH}_2\text{Et} = 6\cdot07$  per cent.

#### *Acid Aniline o-Picraminobenzoate.*

3·5 Grams of *o*-picraminobenzoic acid were dissolved in the smallest possible quantity of cold aniline. After several days, a mass of reddish-yellow crystals separated. These crystals were washed repeatedly with alcohol and with ether in the cold. The yield was 2 grams. The substance consists of reddish-yellow prisms, crystallising in compact masses formed of radiating clusters of crystals. It darkens just below the melting point, and melts and decomposes at 264—265°. It is soluble in water, and is easily hydrolysed by it to the acid. Methyl and ethyl alcohols dissolve the substance sparingly; it is insoluble in ether, and readily soluble in aniline or potassium hydroxide solution:

0·3212 gave 0·0386 Pt.  $\text{NH}_2\text{Ph} = 11\cdot47$ .  
 0·3538 " 0·0424 Pt.  $\text{NH}_2\text{Ph} = 11\cdot44$ .  
 $\text{C}_{22}\text{H}_{23}\text{O}_{16}\text{N}_9$  requires  $\text{NH}_2\text{Ph} = 11\cdot78$  per cent.

#### *Acid Pyridine o-Picraminobenzoate.*

2·5 Grams of *o*-picraminobenzoic acid were dissolved in 2·2 gram of pyridine. After several days, a mass of crystals had formed. The product was washed repeatedly with ether. The yield was 1·4 grams. The crystals are small, yellowish-red, compact, six-sided tables. On heating, the substance loses pyridine at about 140°, and the residue melts at 269° (pure acid 270°). The substance is easily decomposed by water, and also by methyl and ethyl alcohols, acetone, or amyl alcohol, giving the acid. It is insoluble in ether, and has a slight odour of pyridine:

0·2812 gave 0·0364 Pt.  $\text{C}_5\text{H}_5\text{N} = 10\cdot67$ .  
 0·3238 " 0·0410 Pt.  $\text{C}_5\text{H}_5\text{N} = 10\cdot00$ .  
 $\text{C}_{14}\text{H}_{12}\text{O}_{16}\text{N}_9$  requires  $\text{C}_5\text{H}_5\text{N} = 10\cdot20$  per cent.

#### *Acid Sodium m-Picraminobenzoate.*

This salt was prepared as described above for the corresponding ortho-salt. 2·5 Grams of pieryl chloride, 1·7 grams of *m*-amino-

benzoic acid, and 1·2 grams of sodium hydroxide yielding 2·1 grams of the crude product.

It consists of scarlet, elongated plates, not so dark in colour as the ortho-salt. The crystals are somewhat hygroscopic, and are easily hydrolysed by water or by dilute alcohol to the corresponding acid. They are sparingly soluble in alcohol, and insoluble in ether:

0·2874 gave 0·0262  $\text{Na}_2\text{SO}_4$ .  $\text{Na} = 2\cdot95$ .

0·3703 „ 0·0358  $\text{Na}_2\text{SO}_4$ .  $\text{Na} = 3\cdot13$ .

$\text{C}_{26}\text{H}_{15}\text{O}_{16}\text{N}_8\text{Na}$  requires  $\text{Na} = 3\cdot20$  per cent.

#### *Acid Potassium m-Picraminobenzoate.*

1·25 Grams of picryl chloride and 0·7 gram of *m*-aminobenzoic acid were separately dissolved in the least quantity of alcohol, and then a large excess of potassium acetate was stirred into the mixed solutions. After some time, the product was removed and treated as in previous cases. The yield was 1 gram. The substance consists of long, red needles, sparingly soluble in methyl and ethyl alcohols, insoluble in ether, soluble in water, and very easily hydrolysed by it to the acid. It cannot be recrystallised from the usual solvents, owing to the precipitation of the acid with the salt:

0·3370 gave 0·0412  $\text{K}_2\text{SO}_4$ .  $K = 5\cdot48$ .

0·7108 „ 0·0872  $\text{K}_2\text{SO}_4$ .  $K = 5\cdot33$ .

$\text{C}_{26}\text{H}_{15}\text{O}_{16}\text{N}_8\text{K}$  requires  $K = 5\cdot31$  per cent.

#### *Potassium m-Picraminobenzoate.*

3·5 Grams of *m*-picraminobenzoic acid were dissolved in boiling alcohol, and 0·8 gram of potassium hydroxide dissolved in dilute alcohol was stirred into the hot solution. After a short time, the reaction mixture was cooled in ice and salt to  $-10^\circ$  and filtered. In a few days, crystals had separated from the filtrate, and these were collected and washed with alcohol and ether. The yield was 1·9 grams. The substance consists of brilliant pale yellow crystals, and it is sparingly soluble in alcohol and insoluble in ether, but readily so in water to an orange solution. Even after boiling this solution, there is only the faintest indication of hydrolysis to the acid. The acid is precipitated at once on the addition of dilute acid:

0·4595 gave 0·1064  $\text{K}_2\text{SO}_4$ .  $K = 10\cdot38$ .

0·4218 „ 0·1003  $\text{K}_2\text{SO}_4$ .  $K = 10\cdot66$ .

$\text{C}_{15}\text{H}_7\text{O}_8\text{N}_4\text{K}$  requires  $K = 10\cdot10$  per cent.

*The Acid Methylammonium m-Picruminobenzoates.*

2·5 Grams of picryl chloride and 1·4 grams of *m*-aminobenzoic acid were separately dissolved in boiling alcohol. The solutions were mixed, and 2 c.c. of a 33 per cent. methylamine solution added. The solution was well cooled, filtered, and set aside. In a few days two kinds of crystals had separated. The one kind were dark red and transparent, the others were yellowish-red and opaque. These two salts were separated mechanically. Good separation was possible on account of the size of the clusters of crystals.

The dark red crystals consisted of compact tables, crystallising in radiating clusters. The substance has no definite melting point, owing to decomposition on heating. It is completely soluble in hot water to a dark red solution, sparingly soluble in alcohol, and insoluble in ether. The yield was 1·4 grams.

The yellowish-red, opaque crystals also consisted of compact tables, but these melted fairly sharply at 164—166°, with decomposition. This salt is also completely soluble in hot water to a red solution. It is sparingly soluble in alcohol, and insoluble in ether. The yield was 0·9 gram. Analysis showed that both salts have the same composition, and are acid salts:

A. Dark red salt; no definite melting point.

1·3479 gave 0·4031  $(\text{NH}_2\text{Me})_2\text{PtCl}_6$  and 0·0041 Pt.  $\text{NH}_2\text{Me} = 4\cdot62$ .

B. Opaque, yellowish-red salt, melting at 164—166°.

0·4491 gave 0·1214  $(\text{NH}_2\text{Me})_2\text{PtCl}_6$  and 0·0056 Pt.  $\text{NH}_2\text{Me} = 3\cdot9$ .

$\text{C}_{27}\text{H}_{21}\text{O}_{20}\text{N}_9$  requires  $\text{NH}_2\text{Me} = 4\cdot26$  per cent.

*Acid Ethylammonium m-Picraminobenzoate.*

2·5 Grams of picryl chloride, 1·4 grams of *m*-aminobenzoic acid, and 2·5 c.c. of 33 per cent. ethylamine solution, treated as in the previous case, yielded 3 grams of the salt, which was recrystallised from weak alcoholic ethylamine.

The substance crystallises in bright yellow plates, melting at 188°, which are sparingly soluble in alcohol to a red solution, insoluble in ether, and soluble in hot water to a dark red solution. When crystallised from pure alcohol, the salt is decomposed slightly:

0·6135 gave 0·2035  $(\text{NH}_2\text{Et})_2\text{PtCl}_6$  and 0·0036 Pt.  $\text{NH}_2\text{Et} = 6\cdot3$ .

0·3446 „ 0·0951  $(\text{NH}_2\text{Et})_2\text{PtCl}_6$  „ 0·0105 Pt.  $\text{NH}_2\text{Et} = 6\cdot3$ .

$\text{C}_{28}\text{H}_{25}\text{O}_{20}\text{N}_9$  requires  $\text{NH}_2\text{Et} = 6\cdot07$  per cent.

*Acid Guanidine m-Picraminobenzoate.*

3·5 Grams of *m*-picraminobenzoic acid and 0·6 gram of guanidine carbonate, treated by the usual method, gave 2·5 grams of the salt.

The substance is soluble in hot water to a dark red solution without precipitation of the acid. It is sparingly soluble in alcohol, insoluble in ether, and melts at 246°:

n<sub>D</sub><sup>20</sup> 1.76 gave 0.1044 (CH<sub>3</sub>N)<sub>2</sub>H<sub>2</sub>PtCl<sub>6</sub> and 0.0089 Pt. CH<sub>5</sub>N = 7.82.  
C<sub>27</sub>H<sub>21</sub>O<sub>16</sub>N<sub>11</sub> requires CH<sub>5</sub>N = 7.81 per cent.

*Sodium p-Picraminobenzoate.*

1.2 Grams of *p*-picraminobenzoic acid were dissolved in alcohol, to which 10 per cent. of acetone had been added. To the hot solution was added gradually 3.0 c.c. of a 5 per cent. solution of sodium hydroxide in dilute alcohol. After some time, the crystals were collected. The yield was 0.9 gram of a brownish-yellow substance, which crystallises in minute needles. These settled out in tufts on the sides of the vessel. The substance is moderately soluble in alcohol, and insoluble in ether. It is readily and completely soluble in water without any precipitation of the acid. The aqueous solution is of a dark red colour, and the acid is immediately precipitated from it on the addition of an acid:

0.2528 gave 0.0442 Na<sub>2</sub>SO<sub>4</sub>. Na = 5.66.

0.4179 " 0.0759 Na<sub>2</sub>SO<sub>4</sub>. Na = 5.88.

C<sub>15</sub>H<sub>11</sub>O<sub>4</sub>N<sub>4</sub>Na requires Na = 6.21 per cent.

*Acid Potassium p-Picraminobenzoate.*

1.75 Grams of *p*-picraminobenzoic acid, treated with 0.21 gram of potassium hydroxide in a 10 per cent. solution of acetone in alcohol, yielded 0.9 gram of the salt.

The substance consists of buff-coloured needles, sparingly soluble in alcohol, and insoluble in ether. It is moderately soluble in hot water to a dark red solution, and is partly hydrolysed to the acid:

0.4024 gave 0.0485 K<sub>2</sub>SO<sub>4</sub>. K = 5.40.

0.4314 " 0.0512 K<sub>2</sub>SO<sub>4</sub>. K = 5.70.

C<sub>26</sub>H<sub>15</sub>O<sub>16</sub>N<sub>3</sub>K requires K = 5.31 per cent.

*Ammonium p-Picraminobenzoate.*

1.5 Grams of *p*-picraminobenzoic acid, treated in boiling alcohol (200 c.c.) with 2 c.c. of *N*-ammonia solution, yielded, on cooling, 0.7 gram of the salt. The substance crystallises in very dark red needles.

It becomes pale yellow on heating to 210°, and has no well-defined melting point, owing to decomposition on heating. It is sparingly soluble in alcohol, insoluble in ether, and completely soluble in

water to a dark red solution. Analysis showed the substance to be the normal salt:

0·1490 gave 0·0760  $(\text{NH}_4)_2\text{PtCl}_6$  and 0·0025 Pt.  $\text{NH}_4 = 4\cdot44$ .

0·2974 „ 0·1705  $(\text{NH}_4)_2\text{PtCl}_6$  „ 0·0020 Pt.  $\text{NH}_4 = 4\cdot76$ .

$\text{C}_{13}\text{H}_{11}\text{O}_8\text{N}_5$  requires  $\text{NH}_4 = 4\cdot93$  per cent.

*Acid Methylammonium p-Picraminobenzoate.*

1·75 Grams of *p*-picraminobenzoic acid were suspended in 70 c.c. of boiling alcohol, and 0·15 gram of methylamine in dilute alcohol was added. The acid dissolved, and in a few days long, slender reddish-golden coloured needles had separated. The yield was 1·2 grams, and the crystals melted at 204°. They are sparingly soluble in alcohol, insoluble in ether, and readily soluble in warm water to a dark red solution. Analysis showed the substance to be the acid salt:

0·3876 gave 0·1345  $(\text{NH}_2\text{Me})_2\text{PtCl}_6$  and 0·0054 Pt.  $\text{NH}_2\text{Me} = 4\cdot45$ .

0·3764 „ 0·0507 Pt.  $\text{NH}_2\text{Me} = 4\cdot44$ .

$\text{C}_{27}\text{H}_{21}\text{O}_{16}\text{N}_9$  requires  $\text{NH}_2\text{Me} = 4\cdot26$  per cent.

*Hydrolysis of the Acid Potassium Salt of o-Picraminobenzoic Acid.*

The salt was stirred with water in a solubility apparatus at 25° for eight hours. Care was taken that the water was not in excess. The residue, on analysis, was in each case found to contain unaltered salt.

After eight hours, some of the solution was filtered off at the temperature of the thermostat and removed for analysis. The acid was precipitated by a few drops of concentrated hydrochloric acid, collected, and dried, first at 100° and then at 150°. It was then weighed. The filtrate from this treatment was practically colourless, showing that the precipitation of the acid was practically complete. It was evaporated carefully with sulphuric acid, and the potassium in it was estimated as  $\text{K}_2\text{SO}_4$ . From the weights of the acid and the potassium sulphate, the total amounts of the base and the acid radicle in solution were obtained. The concentrations of the hydroxidions and hydrions were calculated from the formulae:

$$(1) \quad C_{\text{OH}} = C_m - \frac{1}{2}(C_r - C_d). \quad (2) \quad C_H = \frac{K_w}{C_{\text{OH}}}$$

The following are the results obtained in three different experiments:

Temperature = 25°.						
Solubility of acid = $1 \cdot 244 \times 10^{-6}$	equivalents per c.c.					
Ionic product for water, $K_w = 1 \cdot 20 \times 10^{-20}$ .						
Weight of solution.	$K_2SO_4$	Acid.	$C_a \times 10^6$	$C_r \times 10^6$	$C^{OH} \times 10^6$	$C_H \times 10^{15}$
29.06	0.0168	0.0586	6.566	5.791	4.291	2.860
25.95	0.0118	0.0522	6.555	5.775	4.290	2.860
29.79	0.0156	0.0527	6.725	5.975	4.510	2.962
			Mean values ...	...	4.363	2.771

It will be noted that the constant concentration of the alkali in solution is very small, and is, roughly,  $N/250$ .

#### Summary.

1. The picraminobenzoic acids form a characteristic series of acid salts, containing two equivalents of the acid radicle to one equivalent of the base.
2. These salts are only moderately soluble in water, and are generally easily hydrolysed, with precipitation of the acid, leaving alkali in solution. The hydrolysis is complete in presence of excess of water, and takes place slowly even in the cold. When the salt is in excess, a state of equilibrium is set up between the salt, acid, and base in solution.
3. The normal salts obtained are readily soluble in water, and show little signs of hydrolysis even on boiling with water.
4. The picraminobenzoic acids are sparingly soluble in water, have very feeble acid properties, and are non associated in solution.

CHEMICAL DEPARTMENT,  
S.W. POLYTECHNIC, CHELSEA, S.W.

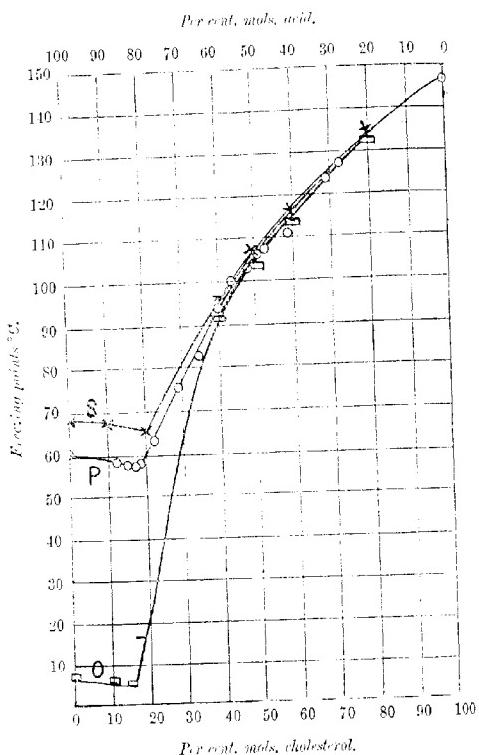
#### XXXIX.—Cholesterol and Fatty Acids.

By JAMES RIDDICK PARTINGTON.

BENEKE (*Ann. Chem. Pharm.*, 1863, **127**, 105) observed that cholesterol which had been crystallised from hot acetic acid "differs from ordinary cholesterol." Lindenmeyer (*J. pr. Chem.*, 1863, **90**, 321, 331) states that he had been informed by Dr. Zalesky that cholesterol crystallises in thin needles from acetic acid, but in plates from other solvents. He prepared crystals in this way, pressed them between filter-paper, and dried "at the ordinary temperature." They melted at 110°, and in two experiments the losses at

120° were 12·7 and 13·7 per cent. The calculated loss for  $C_{26}H_{44}O_2C_2H_4O_2$  was 13·9 per cent., and Lindenmeyer concluded that the substance was an equimolecular compound, the defect in the loss being put down to difficulties in removing the whole of the acetic acid.

F. C. Moore (*Med. Chron.*, 1908, p. 204) quotes the above experi-



ments as evidence for the existence of a compound of cholesterol and acetic acid, and repeated some of the tests. The evidence was:

(1) The different melting points of pure cholesterol and the "compound."

(2) The change of melting point after treating with water, alcohol, or alkalis.

(3) The change of crystalline form after complete dissolution in alcohol, and crystallisation.

Moore and C. P. White (*Med. Chron.*, 1908; *J. Path. Bact.*, 1908, 13, 5) then extended this conclusion (it appears to the author without any satisfactory experimental proof) to other fatty acids, such as palmitic and stearic; the latter author stating that "cholesterol has the remarkable character of being able to take up fatty acids to form loose combinations which are not the esters. Presumably in these combinations the acids exist as 'acids of crystallisation.'"

Since the evidence in the case of acetic acid is not conclusive, and in the cases of stearic and palmitic acids is wanting, I decided, on the suggestion of Dr. A. Lapworth, to make further experiments on the matter. The first cases investigated were the mixtures of cholesterol with palmitic, stearic, and oleic acids.

The method used was to determine the temperatures at which the first portion of solid separated from fluid mixtures of the two components. If any definite solid compound is produced at these temperatures, the curve representing temperature of separation as a function of the fractional molecular composition of the mixture will either exhibit a maximum with two minima corresponding with the so-called eutectics, or mixtures of the solid components, or else will show a sharp break in one branch of the two systems of curves descending to a single eutectic point. If, on the contrary, the substance separating is invariably one of the pure components, and, at a single point, both pure components side by side, the system will consist of two unbroken curves meeting in a eutectic point. The existence of solid solutions, that is, of homogeneous crystals containing both components in proportions which are continuous functions of the proportions existing in the fused mass, has not been suggested, and the work here described has not given any indication that this is to be inferred.

#### EXPERIMENTAL.

##### *Freezing-point Experiments.*

*Apparatus.*--The inner tube of a Beckmann freezing-point apparatus was surrounded by a wide test-tube to serve as an air-jacket. The substances were weighed directly into this tube, and fused by careful heating with a flame. The cork, through which passed a thermometer and a platinum stirrer, was then fitted on, the whole placed in the air-jacket, and the temperature at which solid began to separate was determined.

In no experiment was there any indication of a fluid crystal phase; the mixture remained perfectly clear until freezing com-

menced, when the separating substance was distinctly seen to consist of small solid crystals dispersed through the still liquid mass. No moisture was at any time evolved, and the colour, even at the high temperatures, was never darker than a pale amber-yellow, indicating an absence of decomposition.

*Materials.*—The cholesterol and the fatty acids were pure specimens supplied by Kahlbaum. The oleic acid, which was quite colourless, was frozen out and kept on a porous tile in the ice-chest for twelve hours. It was then allowed to melt in a vacuum desiccator over calcium chloride. The purified acid melted at 6°5<sup>o</sup>; higher melting points (14° according to Gottlieb, *Annalen*, 1846, 57, 38) have been recorded, but there is no reason to believe that the sample used was impure. The cholesterol was dried by heating in an air-oven to 110° for some time, and was kept in a desiccator. The palmitic and stearic acids were used directly.

*Results.*—The tables and accompanying curves show that, when liquid mixtures of cholesterol with palmitic, stearic, and oleic acids, in any proportions, are cooled, the solids separating are invariably one of the pure components, or a mechanical mixture of both pure components. Within the whole range of concentrations and temperatures investigated, there is no evidence of the existence of a solid compound of cholesterol with any one of the acids.

The experiments do not exclude the possibility that in some cases solid compounds may exist at the ordinary temperature, but no substance of this type has been detected. The existence of these, or of solid solutions, could be decided by an examination of the cooling curves over a large range of temperature. Solids of approximately constant composition may doubtless be obtained on cooling solutions of cholesterol and fatty acids saturated with both components, or by other means, but the conclusion that the masses are chemical compounds requires stringent proof, which does not appear yet to have been adduced.

TABLE I.  
*Palmitic Acid + Cholesterol.*

Palmitic acid, per cent.	Cholesterol, per cent.	Molecules of acid, per cent.	Freezing point.
100.0	0.0	100.0	60.0 <sup>o</sup>
83.3	16.7	88.2	58.5
80.0	20.0	85.9	57.5
76.9	23.1	83.3	57.0
74.0	26.0	81.1	57.25
68.3	31.1	74.0	61.1
64.5	35.5	73.2	65.0
62.0	38.0	71.1	73.25
58.8	41.2	65.1	82.5

TABLE I (*continued*).*Palmitic Acid + Cholesterol.*

Palmitic acid, per cent.	Cholesterol, per cent.	Molecules of acid, per cent.	Freezing point.
50.0	50.0	60.0	94.0
48.5	51.5	58.5	97.0
46.1	53.9	56.2	100.0
43.8	56.2	53.9	100.5
42.3	57.7	52.5	103.0
41.5	58.5	51.5	106.0
39.1	60.9	49.2	106.5
37.9	62.1	47.9	107.0

*Second Series.*

50.0	107.0
40.8	111.0
31.7	124.0
27.8	127.0
0	147.0

TABLE II.

*Stearic Acid + Cholesterol.*

Molecules of cholesterol, per cent.	Molecules of acid, per cent.	Freezing point.
0	100	68.5 <sup>2</sup>
10	90	67.0
20	80	65.0
30	60	61.4
50	50	101.7
60	40	115.0
80	20	134.0
100	0	147.0

TABLE III.

*Oleic Acid + Cholesterol.*

Molecules of cholesterol, per cent.	Molecules of acid, per cent.	Freezing point.
0	100	6.5 <sup>1</sup>
10	90	6.0
15	85	5.0
20	80	61.0
40	60	95.9
50	50	107.1
60	40	116.4
80	20	131.0

(The mixture 15: 85 solidified completely at 5.0°, and was therefore the eutectic.)

*Cholesterol and Acetic Acid; Cholesterol and Propionic Acid.*

Some experiments have been made with these systems, but the results have proved inconclusive, since the melting points of the supposed "compounds" corresponded with the points on the freezing curves for mixtures, yet the loss of weight on heating and the acidity were in each case approximately those required by the formula:  $C_{27}H_{40}O_2C_2H_4O_2$ ,  $C_{27}H_{40}O_2C_3H_6O_2$ .

This case can be decided by an examination of the vapour-pressure curves during continual withdrawal of the volatile component, and some experiments, the results of which will shortly be communicated, are in progress to settle this point.

*Colloidal Cholesterol.*

During the course of the work it was observed that a solution of cholesterol in alcohol gave a colloidal solution when added in small quantities to water, with stirring. The alcohol was removed by dialysis, and the colloidal solution has been kept for three months without very much deposition of cholesterol. It was immediately precipitated by mineral acids and alkalis (but not by ammonia), and by ferric, platinic, barium, and calcium chlorides; by zinc, copper, magnesium, and ferrous sulphates; cadmium nitrate, and oxalic acid. Acetic acid and silver nitrate did not precipitate it, but increased the size of the particles. Potassium iodide rendered the solution less opalescent.

O. Porges and E. Neubauer (*Biochem. Zeitsch.*, 1908, 7, 152) prepared a colloidal solution of cholesterol by adding a solution of cholesterol in acetone to water and dialysing. They examined in detail its precipitation by salts, and their results are in agreement with the above. They also concluded that it was an anodic suspensoid.

The solution described above is also an anodic colloid; it was found that cholesterol wandered to the anode in a cataphoresis experiment. Further, the precipitates with ferric chloride and calcium chloride, after washing with hot water, gave, on heating with dilute nitric acid, solutions which contained the cations, but no trace of anion. The precipitate with hydrochloric acid, after washing, did not contain a trace of anion, and on prolonged washing passed again into colloidal solution.

In conclusion, I desire to thank Dr. Lapworth for the interest he has displayed during the course of the work.

SCHUNCK LABORATORY, CHEMICAL DEPARTMENT,  
UNIVERSITY OF MANCHESTER.

XI.— *$\alpha$ -Amino- $\alpha$ -phenylacetamide and Some of its Derivatives.*

By CHARLES HUGH CLARKE and FRANCIS FRANCIS.

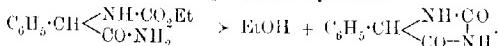
ALTHOUGH Tiemann and Friedländer (*Ber.*, 1881, **14**, 1968) were unable to prepare  $\alpha$ -amino- $\alpha$ -phenylacetamide in a pure state from its hydrochloride, we have found the base is stable, and may be easily obtained from mandelonitrile. The action of alcoholic ammonia on the aldehydecyanohydrins results in the formation of the  $\alpha$ -amino-nitriles, but if the reaction is carried out in the presence of potassium hydroxide, partial saponification of the nitrile group takes place; and, if benzaldehydecyanohydrin is used,  $\alpha$ -amino- $\alpha$ -phenylacetamide is formed, thus:



The isolation of the base from the other products of the reaction is difficult, but if the decomposition is carried out in the presence of benzaldehyde, the well crystalline *benzylidene* derivative can be readily obtained to the extent of about 65 per cent. of the cyanohydrin taken, and  $\alpha$ -amino- $\alpha$ -phenylacetamide is best prepared from it by treating it with phenylhydrazine, when the separation of the resulting benzaldehydecyanoethylhydrazone from the base is easily carried out, and a quantitative yield obtained.

$\alpha$ -Amino- $\alpha$ -phenylacetamide is characterised by the readiness with which it condenses with aromatic aldehydes, forming products of the type  $\text{C}_6\text{H}_5\cdot\text{CH}(\text{N}(\text{CH}_3)\cdot\text{CO}\cdot\text{NH}_2)$ . A similar reaction takes place with acetoacetic ester and ethylacetoacetic ester, but not with the diethyl derivative.

Greater interest lies in the ease with which the five-membered ring, phenylhydantoin, can be formed from the base. The carbethoxy-compound gives an 85 per cent. yield of phenylhydantoin when treated with alcoholic potassium hydroxide:

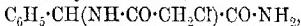


The ease with which the base and its carbethoxy-derivative can be prepared renders this the best method for the preparation of this substance.

Corresponding experiments with  $\alpha$ -amino- $\alpha$ -*p*-methoxyphenylacetamide showed that this also lent itself readily to the formation of *p*-methoxyphenylhydantoin.

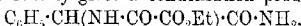
As compared with the ease with which five-membered rings of the above type can be formed is the difficulty experienced in the preparation of any six-membered heterocyclic derivative.

Thus, it was not found possible to obtain a closed ring substance from the interaction of glyoxal and  $\alpha$ -amino- $\alpha$ -phenylacetamide. Further, although chloroacetyl chloride gave a good yield of the corresponding chloroacetyl derivative,



it was again not found possible to eliminate hydrogen chloride and form the six-membered closed chain.

Ethyl oxalate readily gives a condensation product,



but this, on treatment with alcoholic potassium hydroxide or sodium ethoxide, gives the alkali salt of the corresponding acid,  $\text{C}_6\text{H}_5\cdot\text{CH}(\text{NH}\cdot\text{CO}\cdot\text{CO}_2\text{H})\cdot\text{CO}\cdot\text{NH}_2$ , and from this substance and its previously-mentioned ethyl ester we were unable to form any cyclic derivative.

#### EXPERIMENTAL.

##### $\alpha$ -Benzylideneamino- $\alpha$ -phenylacetamide, $\text{C}_6\text{H}_5\cdot\text{CH}(\text{N}\cdot\text{CH}_2\text{C}_6\text{H}_5)\cdot\text{CO}\cdot\text{NH}_2$ .

Ten grams of benzaldehydecyanohydrin and 7 grams of benzaldehyde are dissolved in a small quantity of alcohol, and treated with a mixture of 10 c.c. of a 15 per cent. solution of potassium hydroxide with 10 c.c. of aqueous ammonia (D 0·880).

Sufficient alcohol is then added to give a clear solution. Reaction commences at once, and it is necessary to add small quantities of alcohol from time to time to keep the liquid clear.

After twelve hours, the crystalline condensation product which has separated is collected, washed with ether, and recrystallised from benzene. From this solvent 10 to 12 grams separate on cooling, consisting of colourless plates, melting at 120–121°, insoluble in water, but soluble in hot benzene or alcohol:

0·1842 gave 0·0991  $\text{H}_2\text{O}$  and 0·5126  $\text{CO}_2$ . C = 75·9; H = 5·98.

0·1760 „, 17·7 c.c.  $\text{N}_2$  at 17° and 752 mm. N = 11·6.

$\text{C}_{15}\text{H}_{14}\text{ON}_2$  requires C = 75·6; H = 5·90; N = 11·8 per cent.

##### $\alpha$ -Amino- $\alpha$ -phenylacetamide, $\text{C}_6\text{H}_5\cdot\text{CH}(\text{NH}_2)\cdot\text{CO}\cdot\text{NH}_2$ .

The hydrochloride of this base, previously described by Tiemann and Friedländer, is readily obtained by the action of hydrochloric acid on the benzylidene derivative just described.

As this salt is readily soluble only in hot water, a hot solution must be treated with aqueous potassium hydroxide in order to obtain the base. This treatment results in a partial saponification, and the method consequently gives only a very small quantity of  $\alpha$ -amino- $\alpha$ -phenylacetamide. In this probably lies the explanation for the supposed instability of this base.

On the other hand, the *tartrate* is readily soluble in water, and can be obtained by the decomposition of the benzylidene derivative with a solution of tartaric acid. On removal of the resulting benzaldehyde with ether, the base can be precipitated from a concentrated solution in the cold by means of potassium hydroxide. It may be mentioned here that the tartrate does not lend itself to the separation of the base into its optical components.

The best method for the isolation of the substance in question consists in warming the benzylidene derivative with the calculated amount of phenylhydrazine in benzene solution. The resulting  $\alpha$ -amino- $\alpha$ -phenylacetamide is only sparingly soluble in this medium, and separates first. On cooling, the benzaldehydophenylhydrazone crystallises out, and from this a further amount of base may be extracted by warm water. By this method, a yield of 90 per cent. of the base may be obtained.

$\alpha$ -Amino- $\alpha$ -phenylacetamide is readily soluble in water or alcohol, sparingly so in ether, and almost insoluble in benzene. It is best recrystallised from a mixture of benzene and alcohol, from which it separates on cooling in colourless plates, melting at 130°. Its aqueous solution gives a strongly alkaline reaction, and may be evaporated to dryness without decomposition taking place:

- (1) 0·2024 gave 0·4809 CO<sub>2</sub> and 0·1220 H<sub>2</sub>O. C=64·8; H=6·7.  
0·1920 " 31·0 c.c. N<sub>2</sub> at 16° and 758 mm. N=18·8.  
(2) 0·1620 " 0·3819 CO<sub>2</sub> and 0·0977 H<sub>2</sub>O. C=64·3; H=6·7.  
0·1524 " 24·8 c.c. N<sub>2</sub> at 18° and 750 mm. N=18·6.  
C<sub>8</sub>H<sub>10</sub>ON<sub>2</sub> requires C=64·0; H=6·7; N=18·6 per cent.

$\alpha$ -Amino- $\alpha$ -phenylacetamide readily gives condensation products with aromatic aldehydes similar to the benzaldehyde derivative previously mentioned. These may be prepared in quantitative yield by warming together molecular quantities of the aldehyde with the base in alcoholic solution.

The *salicylidene* derivative, C<sub>6</sub>H<sub>5</sub>·CH(N:CH·C<sub>6</sub>H<sub>4</sub>·OH)·CO·NH<sub>2</sub>, when recrystallised from hot alcohol, melts at 150°:

- 0·2116 gave 0·5506 CO<sub>2</sub> and 0·1140 H<sub>2</sub>O. C=70·9; H=5·98.  
C<sub>15</sub>H<sub>14</sub>O<sub>2</sub>N<sub>2</sub> requires C=70·9; H=5·51 per cent.

The *o-methoxybenzylidene* derivative,

C<sub>6</sub>H<sub>5</sub>·CH(N:CH·C<sub>6</sub>H<sub>4</sub>·OMe)·CO·NH<sub>2</sub>, is not formed so easily as the preceding. When recrystallised from alcohol, it melts at 174–175°:

- 0·2180 gave 20·4 c.c. N<sub>2</sub> at 12° and 750·5 mm. N=10·9.  
C<sub>16</sub>H<sub>16</sub>O<sub>2</sub>N<sub>2</sub> requires N=10·5 per cent.

The *p-methoxybenzylidene* derivative was prepared by heating the alcoholic solution of anisaldehyde and base for some hours

before the condensation was complete. It crystallises from hot alcohol in colourless needles, melting at 164–165°:

0·1894 gave 17·8 c.c. N<sub>2</sub> at 17° and 762 mm. N=10·9.  
 $C_{16}H_{18}O_2N_2$  requires N=10·5 per cent.

*Ethyl  $\beta$ -Carbamylphenylmethylaminocrotonate,*  
 $NH_2CO\cdot CHPh\cdot NH\cdot CMe:CH\cdot CO_2Et$ .

When molecular quantities of acetoacetic ester and the base are heated together in alcoholic solution with a trace of sodium ethoxide, a quantitative yield of the condensation product separates out on the addition of water. It is only sparingly soluble in benzene or ether, and best recrystallised from dilute alcohol, from which it separates in colourless needles, melting at 150°:

0·2814 gave 27·2 c.c. N<sub>2</sub> at 14° and 738 mm. N=11·0.  
 $C_{14}H_{18}O_3N_2$  requires N=10·7 per cent.

Ethylacetoacetic ester gave a corresponding derivative, melting at 132°, which was not analysed, but no condensation product could be obtained from diethylacetoacetic ester.

#### *Preparation of Phenylhydantoin.*

Both the carbomethoxy- and carbethoxy-derivatives of amino-phenylacetamide were prepared and investigated in order to find which condensed more readily to the hydantoin.

*$\alpha$ -Carbomethoxyamino- $\alpha$ -phenylacetamide,*  
 $C_6H_5\cdot CH(NH\cdot CO_2Me)\cdot CO\cdot NH_2$ ,

is readily obtained in quantitative yield by shaking a solution of the base in water containing sodium carbonate with methyl chloroformate. It crystallises from dilute alcohol in colourless plates, melting at 210°, and is readily soluble in hot water or alcohol:

0·1356 gave 16·6 c.c. N<sub>2</sub> at 18° and 751 mm. N=13·9.  
 $C_{10}H_{12}O_3N_2$  requires N=13·4 per cent.

*$\alpha$ -Carbethoxyamino- $\alpha$ -phenylacetamide,*  
 $C_6H_5\cdot CH(NH\cdot CO_2Et)\cdot CO\cdot NH_2$ ,

may be prepared in a similar manner to the previous derivative by employing ethyl chloroformate. It is only sparingly soluble in the ordinary organic solvents, and is best recrystallised from dilute pyridine, from which it separates in small, brilliant needles, melting at 202°:

0·2664 gave 30·4 c.c. N<sub>2</sub> at 22° and 760 mm. N=12·9.  
 $C_{11}H_{14}O_3N_2$  requires N=12·6 per cent.

When this derivative is warmed with dilute hydrochloric acid, it dissolves, and, on cooling,  *$\alpha$ -carbethoxyamino- $\alpha$ -phenylacetic acid*, melting at 118°, crystallises out:

0·1418 gave 8·4 c.c. N<sub>2</sub> at 19° and 749·5 mm. N=6·7.

C<sub>11</sub>H<sub>13</sub>O<sub>4</sub>N requires N=6·3 per cent.

No difference was found in the case with which the carbomethoxy- or carbethoxy-derivative split off methyl and ethyl alcohols respectively to form phenylhydantoin.

When, for instance,  $\alpha$ -carbethoxyamino- $\alpha$ -phenylacetamide was warmed with dilute alcoholic potassium hydroxide, it slowly dissolved, and on diluting with water and acidifying with hydrochloric acid, an 85 per cent. yield of phenylhydantoin (m. p. 178°) was obtained. (Found, N=15·5. Calc., N=15·8 per cent.)

*$\alpha$ -p-Methoxybenzylideneamino- $\alpha$ -p-methoxyphenylacetamide,*  
MeO·C<sub>6</sub>H<sub>4</sub>·CH(N'CH·C<sub>6</sub>H<sub>4</sub>·OMe)·CO·NH<sub>2</sub>.

A 60 per cent. yield of this substance can be obtained by treating a mixture of anisaldehyde and anisaldehydecyanohydrin with a solution of potassium hydroxide and ammonia, as previously described. The derivative, which separates after some time, recrystallises from alcohol and benzene, and melts at 141°:

0·1600 gave 0·4924 CO<sub>2</sub> and 0·0926 H<sub>2</sub>O. C=68·6; H=6·44.

0·1884 „ 16·0 c.c. N<sub>2</sub> at 23° and 751 mm. N=9·45.

C<sub>17</sub>H<sub>13</sub>O<sub>3</sub>N<sub>2</sub> requires C=68·4; H=6·04; N=9·39 per cent.

An 80 per cent. yield of the free base itself,  $\alpha$ -amino- $\alpha$ -p-methoxyphenylacetamide, MeO·C<sub>6</sub>H<sub>4</sub>·CH(NH<sub>2</sub>)·CO·NH<sub>2</sub>, can be obtained from this condensation product by the use of phenylhydrazine in a similar manner to that previously described in the case of the phenyl derivative.

The base is soluble in water, sparingly so in benzene, and may be recrystallised from a mixture of benzene and alcohol, from which medium it is obtained in colourless needles, melting at 134°:

0·1060 gave 14·8 c.c. N<sub>2</sub> at 19° and 748·5 mm. N=15·8.

C<sub>9</sub>H<sub>12</sub>O<sub>2</sub>N<sub>2</sub> requires N=15·6 per cent.

The benzoyl derivative crystallises from alcohol, and melts at 184°:

0·1440 gave 13·2 c.c. N<sub>2</sub> at 23° and 763 mm. N=10·4.

C<sub>16</sub>H<sub>16</sub>O<sub>3</sub>N<sub>2</sub> requires N=9·9 per cent.

The carbethoxy-derivative crystallises from hot water, and melts at 223°:

0·1560 gave 15·6 c.c. N<sub>2</sub> at 20° and 757·5 mm. N=11·4.

C<sub>12</sub>H<sub>16</sub>O<sub>4</sub>N<sub>2</sub> requires N=11·2 per cent.

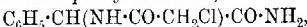
When this substance is treated with alcoholic potassium hydroxide, the solution diluted and acidified in a similar manner to that previously described, an 80 per cent. yield of p-methoxy-

*phenylhydantoin* is obtained. When crystallised from hot water, it melts at 188–189°:

0·1344 gave 16·4 c.c. N<sub>2</sub> at 22·5° and 749 mm. N=13·6.  
 $C_{10}H_{10}O_3N_2$  requires N=13·6 per cent.

The following derivatives were investigated in order to see whether it was possible to prepare six-membered rings from them. In all cases negative results were obtained.

*$\alpha$ -Chloroacetylaminoo- $\alpha$ -phenylacetamide,*



was obtained by the action of chloroacetyl chloride on aminophenylacetamide in benzene solution, in the presence of anhydrous sodium carbonate. The reaction takes place slowly at the temperature of the boiling solvent.

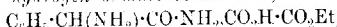
The derivative, which melts at 170°, is only sparingly soluble in benzene or ether, and may be crystallised from hot water and alcohol:

0·2310 gave 20·4 c.c. N<sub>2</sub> at 18° and 741 mm. N=12·7.  
 $C_{10}H_{11}O_2N_2Cl$  requires N=12·4 per cent.

*Reaction with Diethyl Oxalate.*

When the base is warmed for a short time with diethyl oxalate, a solid separates, which, when crystallised from a mixture of alcohol, water, and ethyl acetate, melts and decomposes at 195°.

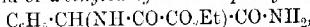
The analysis given below, and the properties, showed that this was the *ethyl hydrogen oxalate* of the base,



probably formed by the presence of a small quantity of water. It was not further investigated:

0·1456 gave 0·2854 CO<sub>2</sub> and 0·0870 H<sub>2</sub>O. C=53·5; H=6·6.  
 $C_{12}H_{16}O_5N_2$  requires C=53·7; H=6·0 per cent.

When the base and diethyl oxalate are heated together for some time, the salt just described, which separates at first, soon dissolves. If this solution is then boiled for one hour, on cooling, a quantitative yield of  *$\alpha$ -ethyloxaylaminoo- $\alpha$ -phenylacetamide*,



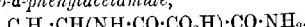
is obtained.

It crystallises from benzene in colourless needles, melting at 116°:

0·1792 gave 17·4 c.c. N<sub>2</sub> at 17·5° and 765 mm. N=11·3.

$C_{12}H_{14}O_4N_2$  requires N=11·2 per cent.

When an alcoholic solution of this condensation product is treated with alcoholic potassium hydroxide, the *potassium salt* of  *$\alpha$ -oxaylaminoo- $\alpha$ -phenylacetamide*,



separates out, and when this is decomposed by acids the free acid itself is obtained.

It is soluble in water or alcohol, and crystallises from ethyl acetate as colourless needles, melting and decomposing at 180°:

0·1782 gave 19·4 c.c. N<sub>2</sub> at 16° and 768 mm. N=12·8.

C<sub>10</sub>H<sub>10</sub>O<sub>4</sub>N<sub>2</sub> requires N=12·6 per cent.

We were unable to form any six-membered cyclic derivatives from this substance or its ethyl ester; various methods usually employed for the purpose, and those which gave almost quantitative yields of hydantoins, yielded negative results in all cases.

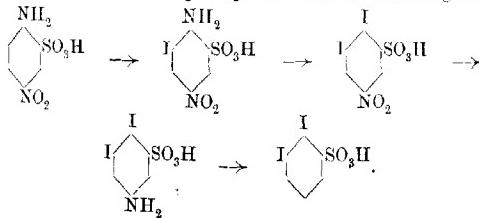
CHEMICAL DEPARTMENT,  
UNIVERSITY OF BRISTOL.

XLI.—*Iodobenzenemonosulphonic Acids. Part III.  
2:3-Di-iodo- and 2:3:4:5-tetraiodo-benzene-sulphonic Acids.*

By MARY BOYLE.

Of the six theoretically possible di-iodobenzenemonosulphonic acids, four were described in 1909 (*Trans.*, **95**, 1683); a fifth, namely, 2:3-di-iodobenzenesulphonic acid, has now been prepared and examined, and is described in the present communication.

When iodine chloride acts on a dilute hydrochloric acid solution of aniline-*o*-sulphonic acid, iodine enters exclusively into the para-position with respect to the amino-group; no trace of an ortho-isomeride can be detected. The latter substance should, however, be easily formed by first substituting the para-hydrogen atom, then introducing iodine into the free ortho-position, and finally removing the para-substituted group. Naturally, the only group that lends itself to ready introduction and elimination in this series of substances is the nitro-group, so that the first step in the synthesis of 2:3-di-iodobenzenesulphonic acid is the preparation of *p*-nitro-aniline-*o*-sulphonic acid, which substance can then be made to undergo the series of changes represented in the following scheme:



These operations proceed quite smoothly, but only moderate yield are obtained in two of the reactions; the other three give excellent results.

*p*-Nitroaniline-*o*-sulphonic acid was originally prepared by Fischer (*Ber.*, 1891, **24**, 3789) by heating 1-chloro-4-nitrobenzene-2-sulphonic acid with alcoholic ammonia in sealed tubes, but the difficulties and dangers in the way of this method of preparation were found to be too great to allow of its employment. It was found extremely difficult to regulate the pressure to that necessary for the displacement of the chlorine by the amino-group; explosions often occurred, and very small quantities only could be worked up at a time.

As a method by which the acid could be prepared readily and in large quantities was essential, attention was first turned to the sulphonation of *p*-nitroaniline and *p*-nitroacetanilide. The latter was subjected to the action of concentrated sulphuric acid and mixtures of concentrated and fuming sulphuric acid, at low and high temperatures, under ordinary pressure and in sealed tubes, but no sulphonation could be effected; either *p*-nitroaniline was recovered, or complete carbonisation occurred.

The nitration of aniline-*o*-sulphonic acid under varying conditions was then undertaken, and carried through successfully. By employing the acetylated derivative in the form of its barium salt and lowering the temperature considerably, a mononitro-derivative was isolated without difficulty.

The influence of temperature on the reaction is very marked, a few degrees making the difference between a good and a poor yield. For example, when the solution of the acetylated barium salt in concentrated sulphuric acid was cooled in ice, and the temperature kept at 10–15° during the addition of the requisite amount of nitric acid, the yield of nitro-acid amounted to 46·6 per cent.; when, however, the acid solution was cooled in a freezing mixture and the temperature never allowed to rise above 7°, the yield amounted to 80 per cent. of the theoretical.

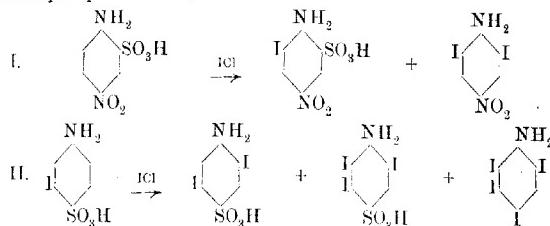
That the nitro-group displaces the hydrogen in the para-position with respect to the amino-group was proved by first displacing the latter group by iodine, then reducing the nitro-group and displacing it by iodine; in this way 2:5-di-iodobenzenesulphonic acid was obtained and identified by its appearance and the melting point of its chloride.

It is interesting to note that the isomeric acetanilide-*m*-sulphonate, which is nitrated at the ordinary temperature, 15–20°, cannot be nitrated at a temperature much below this, an attempt to improve the yield of this acid by carrying out the

operation at the low temperature essential for the formation of the *o*-nitro-isomeride proving unsuccessful.

The introduction of iodine into *p*-nitroaniline-*o*-sulphonic acid is readily brought about by the action of iodine chloride, but a secondary reaction, in which the sulphonic group is displaced by iodine, also occurs to some extent, so that a mixture of 2-iodo-4-nitroaniline-*o*-sulphonic acid and 2:6-di-iodo-4-nitroaniline is obtained. The amount of the latter substance, however, may be very considerably reduced by careful regulation of the experimental conditions.

The displacement of a sulphonic group by an iodine atom has been observed during the iodination, not only of the above nitro-substituted aniline-*o*-sulphonic acid, but also of an iodo-substituted aniline-*p*-sulphonic acid, thus:



Since the sulphur-free product occurs to a considerable extent in both cases and cannot escape detection, it is remarkable that in the earlier experiments on the iodination of the unsubstituted anilinesulphonic acids described in Part I, iodoanilines should not have been detected. In order to discover whether an tri-iodoaniline could be formed by the action of iodine chloride on aniline-*p*-sulphonic acid, an experiment was conducted in which a dilute solution of the latter was subjected to a large excess of the reagent. After concentrating the solution, the solid which separated from the cooled liquid was found to consist mainly of di-iodoaniline-sulphonic acid, together with a small quantity of a purplish-black substance free from sulphur; examination has made clear that the latter substance is not 2:4:6-tri-iodoaniline. Similarly, aniline-*p*-sulphonic acid does not yield an iodoaniline when treated with iodine chloride under ordinary experimental conditions, whilst under all conditions the sulphonic group in aniline-*m*-sulphonic acid remains unattacked.

It is clear, then, that the action of iodine chloride is comparable only to a certain extent with that of chlorine and bromine on unsubstituted amino-sulphonic acids, in which interactions the ortho- and para-isomerides yield mixtures of halogenated amino-sulphonic acids

and tri-halogen-substituted anilines, and the meta-isomeride yields halogenated aminosulphonic acids only.

Brenzinger (*Zeitsch. angew. Chem.*, 1896, **9**, 131) states that the action of bromine on the para-compound is quantitatively to displace the sulphonate group, so that the acid may be estimated by determining the sulphuric acid set free; iodine, on the other hand, only displaces the sulphonate group readily from substituted aniline-sulphonic acids, and the action does not proceed to completion.

The diazotisation of 2-iodo-4-nitroaniline-*o*-sulphonic acid proceeds smoothly, and a quantitative yield of the di-iodo-acid in the form of its potassium salt is obtained when the diazo-anhydride is decomposed with potassium iodide.

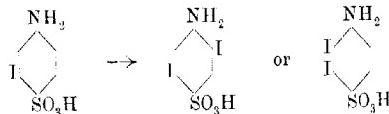
The greatest loss of material occurs during the reduction of the nitro-group, and the displacement of the amino-group by hydrogen by the diazo-reaction. Two methods of reduction have been employed, the first involving the use of ferrous hydroxide, the second that of stannous chloride in hydrochloric acid; the latter method is the more convenient, since the operation is speedy and takes place at 100°.

Up to the present, no experiments have resulted in a yield of di-iodosulphonic acid greater than 50 per cent. of the di-iodoamino-sulphonic acid employed.

The di-iodo-acid obtained in this way is a crystalline substance, which melts at 147–148°, and gives rise to a well-characterised chloride, melting at 127°.

An attempt has been made to prepare 2:3-di-iodobenzene-sulphonic acid in another way, and although the experiments have not been successful so far as their initial purpose is concerned, they have led to some interesting results in other directions.

When *m*-idoaniline-*p*-sulphonic acid is subjected to the action of one molecular proportion of iodine chloride, the iodine atom introduced may occupy one of two positions, both ortho- to the amino-group; the resulting product therefore is either 2:5-di-iodoaniline-*p*-sulphonic or 2:3-di-idoaniline-*p*-sulphonic acid:



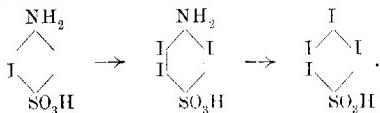
There is the third alternative that a mixture of the two acids may be produced, in which case a separation might be effected, and the 2:3-di-idoaniline-sulphonic acid converted into the desired 2:5-di-iodobenzenesulphonic acid by eliminating the amino-group.

Experimental results, however, make clear that only one position

is available for the entering iodine atom, and 2:5-di-iodoaniline-*p*-sulphonic acid is the sole product of the reaction. This fact was proved by concentrating the liquid that had been submitted to the action of the iodine chloride, collecting at intervals the crystals which separated from the cooled liquid until three or four sets of crystals had been obtained, and then displacing the amino-group in each of these by an iodine atom; each set of crystals yielded, in this way, 2:4:5-tri-iodobenzenesulphonic acid, which gave rise to a sulphonyl chloride melting sharply, even without purification, at 135°.

Confirmatory proof of the position taken up by the iodine was obtained by the production of 2:5-di-iodobenzenesulphonic acid on displacing the amino-group by hydrogen.

In some experiments the successful introduction of iodine into the second ortho position seemed to have been achieved when a crop of more soluble crystals were found, on displacing the amino-group by iodine, to yield an iodo-sulphonic acid differing from any di- or tri-iodo-acid obtained previously. The acid, however, which is more coloured than any others and is not quite so readily soluble in water, yields a yellow chloride, melting at 163°, and proves on examination and analysis to be a tetraiodobenzenesulphonic acid, formed, without doubt, as follows:



The sparing solubility of 3-iodoaniline-*p*-sulphonic acid in water at the ordinary temperature is a difficulty in the way of preparing the tetraiodo-acid, but, as the solubility increases very considerably with temperature, and as iodine chloride undergoes no appreciable decomposition on being passed into hot aqueous solutions, the iodination may be carried out very satisfactorily at a temperature of 70–75°; under these conditions, two molecules of iodine chloride give rise to 2:3:6-tri-iodoaniline-*p*-sulphonic acid mixed with a little 2:3:4:6-tetraiodoaniline.

#### EXPERIMENTAL.

##### *Preparation of p-Nitroaniline-*o*-sulphonic Acid.*

Fifteen grams of barium acetanilide-*o*-sulphonate were dissolved in 75 grams of concentrated sulphuric acid, and cooled in ice and salt to 3°; a solution of 4.65 c.c. of concentrated nitric acid (D 1.430) in twice its volume of sulphuric acid was then added gradually, the temperature being kept at 3–7°. The addition

occupied about two hours, after which the acid liquor was allowed to remain in the mixture for another hour, and then poured into chopped ice; a clear, pale yellow liquid was obtained. This was neutralised with barium carbonate, and the clear filtrate evaporated to crystallisation, when an orange-yellow barium salt separated:

0·2347 gave 0·0905 BaSO<sub>4</sub>. Ba=22·68.

C<sub>11</sub>H<sub>10</sub>O<sub>10</sub>N<sub>4</sub>S<sub>2</sub>Ba<sub>2</sub>H<sub>2</sub>O requires Ba=22·76 per cent.

The barium salt was decomposed with dilute sulphuric acid, and the acid filtrate evaporated; after concentrating to a very small bulk, the cooled liquid solidified to a mass of pale yellow needles of the nitroaminosulphonic acid, which were collected and drained on porous plate.

To prove the presence of one nitro-group only, the amino-acid was diazotised and the diazo-group displaced by iodine; the potassium 2-*iodo-4-nitrobenzenesulphonate* separated in pale yellow needles, which were purified, dried, and analysed:

0·1658 gave 5·3 c.c. N<sub>2</sub> at 15° and 775 mm. N=3·86.

C<sub>6</sub>H<sub>3</sub>O<sub>5</sub>NISK requires N=3·82 per cent.

#### *2-Iodo-4-nitroaniline-o-sulphonic Acid.*

Twenty grams of *p*-nitroaniline-o-sulphonic acid were dissolved in approximately 500 c.c. of water, 5 c.c. of concentrated hydrochloric acid were then added, and 15 grams of iodine chloride passed into the solution at the ordinary temperature. The yellow colour deepened to red, and a fine yellow powder gradually separated. (In some experiments under slightly different conditions, this precipitate only appeared after some time, but all experiments yielded it to some extent.) After about an hour, the solution was separated from the yellow powder and evaporated, during which operation crystals separated until further concentration was rendered impossible owing to the violent bumping. The filtrate from these crystals yielded, on almost complete evaporation, a mass of bright yellow needles of *2-iodo-4-nitroaniline-o-sulphonic acid*. The potassium salt crystallises in bright yellow, the sodium in darker yellow needles. The former was analysed:

0·1368 gave 0·0963 CO<sub>2</sub> and 0·0137 H<sub>2</sub>O. C=19·19; H=1·11.

C<sub>6</sub>H<sub>3</sub>O<sub>5</sub>N<sub>2</sub>ISK requires C=18·84; H=1·05 per cent.

The yellow crystals separating first were almost insoluble in water, crystallised in needles from alcohol, and were sparingly soluble in benzene. They contained nitrogen, but were devoid of sulphur, and melted at 244°. Analysis showed them to consist of

2: 6-di-iodo-4-nitroaniline, the melting point of which is given by Michael as 244°. (Found, C=18.91; H=1.11. Calc., C=18.95; H=1.05 per cent.)

In order to free 2-iodo-4-nitroaniline-*o*-sulphonic acid from the accompanying 2: 6-di-iodo-4-nitroaniline, the mixture was boiled with sodium carbonate, and the sodium salt crystallised out from the clear filtrate; this sodium salt was then dried, and used instead of the acid itself in the next operation.

Under the best conditions a yield of 71 per cent. of the iodo-nitroaminosulphonic acid was obtained—under ordinary conditions only about 53 per cent.

#### 2: 3-Di-iodo-5-nitrobenzenesulphonic Acid.

Ten grams of sodium 2-iodo-4-nitroaniline-*o*-sulphonate were dissolved in water, and poured into excess of dilute sulphuric acid; the acid mixture was then cooled to 10°, and diazotised by the addition of 2 grams of sodium nitrite. On adding potassium iodide to the flocculent, pale yellow diazo-compound, nitrogen was at once evolved, and an aerated scum rose to the surface of the liquid; after an hour's heating on the water-bath, the precipitate was collected and purified by recrystallisation from water. It crystallises in pale yellow or cream-coloured needles, sparingly soluble in cold water.

The potassium salt yields an insoluble barium salt, from which the acid is obtained in silky needles by addition of sulphuric acid and subsequent concentration.

The sodium salt crystallises in woolly needles; the ammonium salt in small, pale yellow needles.

When the acid is heated in the steam-oven for a short time it becomes almost colourless, but the yellow colour is rapidly restored on exposure to moist air.

A quantitative examination of the acid and its derivatives has not yet been made.

#### 4: 5-Di-iodoaniline-*m*-sulphonic Acid.

In one series of experiments, the nitro-group was reduced by means of ferrous hydroxide. Eight grams of the potassium salt of the nitro-acid were dissolved in about a litre of hot water, 30 grams of crystallised ferrous sulphate were added, and ferrous hydroxide was then precipitated by the addition of 15 grams of potassium hydroxide. The mixture was heated on the water-bath during four hours, after which the ferric hydroxide was separated, and the di-iodoamino-acid precipitated from the filtrate by hydro-

chloric acid. It separates in small, reddish-brown needles which are sparingly soluble in hot water.

The second method of reduction consisted in the use of stannous chloride. The finely-divided potassium salt of the nitro-acid (5 grams) was heated on the water-bath with dilute hydrochloric acid; a solution of stannous chloride in concentrated hydrochloric acid (8 grams in 20 c.c.) was then added, and the mixture was kept at 100° until the yellow nitro-acid had given place to the colourless, powdery amino-acid; the operation takes from half an hour to one hour. The amino-acid was collected, washed, and freed from insoluble matter by solution in alkali and reprecipitation with acid.

*2 : 3-Di-iodobenzenesulphonic Acid.*

The amino-group in 4 : 5-di-iodoaniline-*m*-sulphonic acid was displaced by hydrogen by boiling its diazo-anhydride with alcohol. By carrying out the diazotisation in the minimum amount of dilute sulphuric acid, it was found possible to obtain a large percentage of the diazo-salt in an insoluble condition; on boiling this diazo-salt with methylated spirit, a deep red colour was developed, and after removal of the alcohol, the sodium salt was precipitated from the aqueous solution of the residue by the addition of sodium chloride.

The barium salt is very sparingly soluble; on decomposition with sulphuric acid, it yields the acid in shining crystals, which melt at 147—148°.

The acid yields a well-characterised chloride, which separates from ether in large crystals, and melts at 127°:

0·1727 gave 0·059 CO<sub>2</sub> and 0·0118 H<sub>2</sub>O. C=16·73; H=0·75.

C<sub>6</sub>H<sub>3</sub>O<sub>2</sub>Cl<sub>2</sub>S requires C=16·80; H=0·70 per cent.

*Ethyl 2 : 3-di-iodobenzenesulphonate* separates from ether in stout needles, melting at 77—78°:

0·0726 gave 0·0582 CO<sub>2</sub> and 0·0119 H<sub>2</sub>O. C=21·86; H=1·81.

C<sub>8</sub>H<sub>5</sub>O<sub>3</sub>I<sub>2</sub>S requires C=21·92; H=1·83 per cent.

*Methyl 2 : 3-di-iodobenzenesulphonate* separates from ether in glistening crystals, melting at 101°:

0·1313 gave 0·095 CO<sub>2</sub> and 0·0162 H<sub>2</sub>O. C=19·73; H=1·37.

C<sub>7</sub>H<sub>6</sub>O<sub>3</sub>I<sub>2</sub>S requires C=19·81; H=1·41 per cent.

The *sodium* salt crystallises in needles with one molecule of water of crystallisation:

0·1550 gave 0·0895 CO<sub>2</sub> and 0·0146 H<sub>2</sub>O. C=15·75; H=1·04.

C<sub>6</sub>H<sub>3</sub>O<sub>3</sub>I<sub>2</sub>Na<sub>2</sub>H<sub>2</sub>O requires C=16·00; H=1·11 per cent.

The *potassium* salt separates from water in sparkling plates containing one molecule of water of crystallisation:

0·1602 gave 0·0903 CO<sub>2</sub> and 0·0175 H<sub>2</sub>O. C=15·37; H=1·21.

C<sub>6</sub>H<sub>3</sub>O<sub>3</sub>I<sub>2</sub>SK<sub>2</sub>H<sub>2</sub>O requires C=15·45; H=1·07 per cent.

*2: 3: 4: 5-Tetraiodobenzenesulphonic Acid.*

*m*-Iodoaniline-*p*-sulphonic acid was prepared from 5-nitroaniline-*n* sulphonic acid by the method described in the first communication on this subject (Trans., 1909, 95, 1709). Owing to its very sparing solubility (one litre of water dissolving less than one gram at 20°), further iodination of the substance was carried out at a much higher temperature. Five grams were dissolved in about two litres of water heated to 80—90°, a little hydrochloric acid was added, and two molecular proportions of iodine chloride were then passed rapidly into the hot solution. There was a slight deepening of the yellow colour, and before the full amount had been passed in, a faint turbidity made its appearance. At this point the action was stopped, and the reaction mixture was kept for several hours, after which the grey powder was collected, and the clear filtrate evaporated to one-third its bulk. The crystals which separated from the cooled liquid were freed from neutral insoluble material by dissolving them in sodium carbonate solution; concentrated hydrochloric acid reprecipitated 2: 3: 6-tri-iodoaniline-*p*-sulphonic acid in greyish-white needles. The grey powder, insoluble in water and in sodium carbonate solution, did not contain sulphur, and crystallised from glacial acetic acid in small nodules, and from benzene in fine, woolly needles, melting at 163°:

0·2118 gave 0·0921 CO<sub>2</sub> and 0·0107 H<sub>2</sub>O. C=11·85; H=0·56.

C<sub>6</sub>H<sub>3</sub>N<sub>1</sub>I<sub>4</sub> requires C=12·06; H=0·50 per cent.

The substance is therefore 2: 3: 4: 6-tetraiodoaniline.

Sodium 2: 3: 6-tri-iodoaniline-*p*-sulphonate was then dissolved in water, poured into excess of dilute sulphuric acid, and diazotised; on decomposing the diazo-salt with potassium iodide, potassium 2: 3: 4: 5-tetraiodobenzenesulphonate separated in fine needles.

2: 3: 4: 5-Tetraiodobenzenesulphonyl chloride is pale yellow in colour; it crystallises from ether in small, woolly needles, melting at 161—162°:

0·1150 gave 0·0445 CO<sub>2</sub> and 0·002 H<sub>2</sub>O. C=10·55; H=0·19.

C<sub>6</sub>HO<sub>2</sub>ClI<sub>4</sub>S requires C=10·58; H=0·14 per cent.

The sodium, potassium, and ammonium salts crystallise in small, cream-coloured needles; they are very sparingly soluble in water.

**XLII.—The Mechanism of Doebe[n] and von Miller's  
Quinaldine Synthesis.**

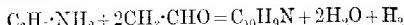
By HUMPHREY OWEN JONES and PERY EDWIN EVANS.

DURING the examination of the case of supposed stereoisomerism described by von Miller and Plöchl (*Ber.*, 1896, **29**, 1462), of the aldol bases,  $C_{12}H_{17}ON$ , derived from *m*-4-xylidine, in which it was shown (Jones and White, *Trans.*, 1910, **97**, 632) that this isomerism was structural, the change of these compounds into 2:6:8-trimethylquinoline by heat and by acids in the cold was studied. This change may be represented by the equation:



but it was found to take place without perceptible evolution of gas at temperatures above the melting point of the base and also in acid solution. The change was then carried out at  $160^\circ$  in an exhausted vessel connected with a Töpler pump, but even when the change was complete no gas had been produced.

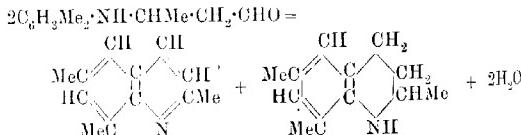
Doebe[n] and von Miller's well-known quinaldine synthesis in presence of concentrated hydrochloric acid is usually represented by the equation:



The hydrogen in this case is found to be used in reducing some of the aldehyde, and, to a less extent, in reducing some of the quinaldine to tetrahydroquinaldine. Now the aldol bases, like many amino-aldehydes and ketones, were found not to be affected by nascent hydrogen produced from sodium and alcohol or water.

Since no hydrogen is evolved, it follows therefore either that the product formed is a derivative of dihydroquinoline, or that it consists of a mixture in equimolecular proportions of a quinoline and a tetrahydroquinoline derivative.

Experiment showed that the latter alternative was correct, and the change is represented by the equation:



either when brought about by heating to  $140$ — $250^\circ$  or by treatment with acids.

The apparent transference of two atoms of hydrogen from one molecule to another in a quantitative manner is interesting, and

it was decided to study the reaction more fully in the hope of elucidating the mechanism by which this transference was effected.

The aldol bases are probably formed as one of the intermediate stages in Doeblner and von Miller's quinaldine synthesis, and the investigation of the above change might therefore throw light on the mechanism of this important synthesis.

The present paper contains an account of the conversion of the  $\alpha$ - and  $\beta$ -aldol bases,  $C_{12}H_{17}ON$ , obtained from *m*-4-xylylidine, into 2:6:8-trimethylquinoline and 2:6:8-trimethyltetrahydroquinoline, and of the properties of these substances and of their derivatives.

The aldol base,  $C_{11}H_{15}ON$ , obtained from *p*-toluidine has been shown to behave similarly when heated or treated with dilute acid, yielding a mixture of 2:6-dimethylquinoline and 2:6-dimethyltetrahydroquinoline.

The aldol bases derived from aniline are not known.

It has also been found that the bimolecular ethyleneketoxylidine,  $C_{20}H_{20}N_2$ , is stable towards heat, and distils unchanged, but that when treated with acids it is very rapidly converted into a mixture in equimolecular proportions of *m*-4-xylylidine, 2:6:8-trimethylquinoline, and 2:6:8 trimethyltetrahydroquinoline.

This last-mentioned reaction, if applied to the case of aniline, yields the corresponding mixture of aniline, quinaldine, and tetrahydroquinaldine.

#### EXPERIMENTAL.

##### *The Action of Heat on the Aldol Bases.*

The aldol bases were prepared by the method previously described (*loc. cit.*, p. 635), and it was ascertained by heating about 0.2 gram of the pure  $\alpha$ - and  $\beta$ -bases in a vacuum to 160° for six hours, that less than 0.1 c.c. of gas was obtained, whereas from the equation  $C_{12}H_{17}ON = C_{12}H_{15}N + H_2O + H_2$  about 24 c.c. of gas should have been evolved. The product in each case was liquid, and consisted of a mixture of a substance which reacted with benzoyl chloride and with nitrous acid and a substance which did not so react.

Similar experiments made with about 0.3 gram of the hydrochloride of the  $\alpha$ - and  $\beta$ -compounds showed that no gas was evolved, although the product now gave none of the original crystalline base when neutralised.

Experiments were therefore made in which large quantities of the mixed  $\alpha$ - and  $\beta$ -aldol bases were heated or treated with acid, and the resulting liquid basic product separated into its constituents, either by treatment with benzoyl chloride and alkali and washing the resulting product with acid, or by dissolving in acid and treating with dilute solution of sodium nitrite. The former method is to be preferred.

Two such experiments may be quoted as typical. 12·5 Grams of the mixed  $\alpha$ - and  $\beta$ -compounds were heated to about 200° for six hours, and yielded 11·0 grams of liquid product, which, when distilled, gave 10·1 grams of a liquid boiling at 150—160°/20 mm.

From this were obtained 6·1 grams of a benzoyl derivative, corresponding with 3·8 grams of base assumed to be 2: 6: 8-trimethyltetrahydroquinoline and 4·9 grams of 2: 6: 8-trimethylquinoline. This shows that 50 per cent. of the base is 2: 6: 8-trimethylquinoline, and the remainder had reacted with benzoyl chloride.

An experiment with  $\alpha$ -*d*-camphorsulphonic acid may be quoted as typical of those made with acids. In the previous paper (*loc. cit.* p. 639) it was found, in attempting to prepare the  $\alpha$ -*d*-camphorsulphonates of the  $\alpha$ - and  $\beta$ -aldol bases in acetone solution, that these were transformed almost immediately, and the camphorsulphonate of 2: 6: 8-trimethylquinoline separated from the solution. This is more sparingly soluble than the camphorsulphonate of 2: 6: 8-trimethyltetrahydroquinoline.

11·3 Grams of the  $\beta$ -aldol base, dissolved in ethyl acetate, were mixed with 13·8 grams of camphorsulphonic acid, also in ethyl acetate, and the solution was evaporated. The residual mass, which crystallised on keeping and weighed 24 grams, was treated with alkali, and the two bases separated as described above. 4·9 Grams of trimethylquinoline and 7·1 grams of benzoyl derivative, corresponding with 4·5 grams of trimethyltetrahydroquinoline, were obtained, showing that the two bases were present in approximately equal quantities. The benzoyl compound obtained was found to separate from alcohol in colourless, well-formed, six-sided prisms, which melt at 143°:

0·1795 gave 0·5201 CO<sub>2</sub> and 0·1185 H<sub>2</sub>O. C=81·3; H=7·55.  
 $C_{19}H_{21}ON$  requires C=81·7; H=7·53 per cent.

It may therefore be concluded that the compound is 1-*benzoyl* 2: 6: 8-trimethyltetrahydroquinoline. The base recovered from the benzoyl derivative by boiling with concentrated hydrochloric acid solution and treating the acid solution with alkali was found to boil at 260—261°/780 mm. and at 142—143°/14 mm. (compare Panajotoff, *Ber.*, 1887, **20**, 34). The distillate solidified on keeping, and the crystals, which were rhombs or six-sided plates, melted at 50—51°. (Found, C=81·8; H=9·63. Calc., C=82·2; H=9·71 per cent.)

This substance was shown to be identical with that obtained by the reduction of 2: 6: 8-trimethylquinoline with sodium and alcohol, and is therefore 2: 6: 8-trimethyltetrahydroquinoline. The

the substance was recovered from the nitroso-compound by treatment with tin and hydrochloric acid.

In order to prepare larger quantities of it, the method adopted was to heat the mixture of aldon bases to 200—250° for four to six hours, to distil off the mixture of bases thus formed (this distillation may be dispensed with without affecting the result), and to reduce the whole by means of sodium and alcohol. The yield is almost quantitative.

The following derivatives of 2: 6: 8-trimethyltetrahydroquinoline have been prepared:

The *hydrochloride* separates from water in stout prisms, melting at 208—209°:

0·5001 gave 0·3320 AgCl. Cl=16·5.

$C_{12}H_{17}N \cdot HCl$  requires Cl=16·78 per cent.

The platinichloride is precipitated as very minute, buff-coloured prisms on the addition of platinic chloride to a solution of the hydrochloride, and melts at 210°.

The *hydrobromide* forms colourless prisms, melting at 222—223°.

The  $\alpha$ -d-camphorsulphonate crystallises from acetone, in which it is very soluble, in long needles, melting at 230°.

The  $\alpha$ -d-broncamphorsulphonate crystallises from acetone in plates, melting at 194—195°.

The *picroate* separates from a mixture of the calculated quantities of the base and picric acid dissolved in alcohol in long, bright yellow prisms, melting at 179°:

0·1773 gave 21·1 c.c. N<sub>2</sub> (moist) at 18° and 736 mm. N=13·5.

$C_{12}H_{20}O_7N_4$  requires N=13·9 per cent.

1-Ethyl-2: 6: 8-trimethyltetrahydroquinoline crystallises from alcohol in colourless, micro-crystalline needles, melting at 108—109°.

1: 2: 6: 8-Tetramethyltetrahydroquinoline *hydriodide* was formed as a solid, crystalline mass from a mixture of methyl iodide and 2: 6: 8-trimethyltetrahydroquinoline in molecular proportions. It separates from hot alcoholic solution in stellate aggregates of colourless prisms, which melt at 168—169°:

0·2645 gave 0·4760 CO<sub>2</sub> and 0·1500 H<sub>2</sub>O. C=49·0; H=6·2.

$C_{12}H_{20}NI$  requires C=49·2; H=6·31 per cent.

1: 2: 6: 8-Tetramethyltetrahydroquinoline separates from the above salt on treatment with alkali as an almost colourless oil, boiling at 256—257°/775 mm.:

0·2835 gave 0·8540 CO<sub>2</sub> and 0·2543 H<sub>2</sub>O. C=82·2; H=9·96.

$C_{12}H_{19}N$  requires C=82·5; H=10·0 per cent.

The *picroate* of the base separates from alcohol in long, lustrous, yellow prisms, melting at 190—191°.

The *platinichloride* is precipitated as buff-coloured needles on the addition of platinic chloride to a solution of the base in hydrochloric acid; it melts and decomposes at 205°.

*1-Benzyl-2: 6: 8-trimethyltetrahydroquinoline hydriodide* is deposited slowly from a mixture of benzyl iodide and 2: 6: 8-trimethyltetrahydroquinoline. It separates from alcohol in long needles, melting and decomposing at 227°:

0·1901 gave 0·1130 AgI. I=31·8.

$C_{19}H_{24}NI$  requires I=33·3 per cent.

The available information concerning 2: 6: 8-trimethylquinoline (Panajotoff, *loc. cit.*) is scanty, so the following additional facts are recorded here.

The base itself crystallises readily in rhombs or diamond-shaped plates, melting at 45—46°, and boiling at 266—267°/780 mm. (Panajotoff gives 260°/719 mm.).

The hydrochloride and *hydrobromide* form colourless prisms, melting at 207° and 172—173° respectively.

The *hydriodide* crystallises in stout, yellow prisms, melting at 223—224°.

The platinichloride is a buff-coloured, micro-crystalline powder, melting at 206—207°.

The picrate forms bright yellow prisms, melting at 187—189°.

The *a-d-camphorsulphonate* melts at 231—232°.

It has also been shown that the corresponding aldol bases formed from *p-toluidine* and acetaldehyde in acid solution (*loc. cit.*, p. 643) are transformed, on heating alone or on treatment with acids, into a mixture of 2: 6-dimethylquinoline (*p-toluquinidine*) and 2: 6-dimethyltetrahydroquinoline in equimolecular proportions.

It has been found that the bimolecular ethyleneketoxime,  $(C_{10}H_{13}N)_2$ , which can be produced from the aldol bases and *m-4-xylylidine*, or from the latter and acetaldehyde in alcohol solution (*loc. cit.*, p. 640), when treated with acids, is very rapidly transformed into a mixture of the salts of xylidine, 2: 6: 8-trimethylquinoline, and 2: 6: 8-trimethyltetrahydroquinoline; xylidine can be separated from the quinoline derivatives by distillation, and the two last are then separated as described above. The aldol bases from aniline have not been prepared, but this modification allows of the synthesis of 2-methylquinoline (quinidine) and its tetrahydro-derivative from aniline by the following process.

One hundred grams of aniline are treated at 0° with 50 c.c. of commercial "concentrated" acetaldehyde with continual stirring; the resulting viscous mass is at once dissolved in about 800 c.c. of hydrochloric acid (about 5*N*), and heated to 100° for an hour. The solution is rendered alkaline, and the bases are separated and

## FORMATION OF 4(OR 5)- $\beta$ -AMINOETHYLGlyOXALINE. 339

distilled. Fifty grams of aniline are recovered, and about 25 grams of a mixture of bases, boiling at 235—255°, are obtained. This mixture was separated by benzoylating and removal of the 2-methyl-quinoline by means of acid, and in two experiments 4·8 and 4·9 grams of 2-methylquinoline were obtained from 10 grams of the mixture. The benzoyl derivative of 2-methyltetrahydroquinoline, melting at 119—120°, was also isolated, thus showing that 2-methyl-quinoline and its tetra-hydro-derivative had been produced in equimolecular quantities.

Commercial "quinaldine" always contains some of the tetra-hydro-derivative, and a specimen obtained from the Actien Gesellschaft für Anilin-Fabrikation was found to contain about 14 to 16 per cent.

The expenses of this work were partly defrayed by means of grants received from the Government Grant Committee of the Royal Society, for which we are glad to make this grateful acknowledgment.

UNIVERSITY CHEMICAL LABORATORY,  
CAMBRIDGE.

### XLIII.—*Experiments on the Formation of 4(or 5)- $\beta$ -Aminoethylglyoxaline from Histidine.*

By ARTHUR JAMES EWINS and FRANK LEE PYMAN.

4(or 5)- $\beta$ -AMINOETHYLGlyOXALINE, the base derived from the naturally occurring amino-acid histidine ( $\alpha$ -amino- $\beta$ -glyoxaline-4(or 5)-propionic acid) by the removal of carbon dioxide from the latter has recently become of considerable interest and importance on account of its occurrence in extracts of ergot (Barger and Dale, Trans., 1910, **97**, 2592) and very great physiological activity (Dale and Laidlaw, *J. Physiol.*, 1910, **41**, 318). It has hitherto been obtained by two methods: (1) by synthesis; (2) by the action of putrefactive organisms on histidine itself.

The base was first synthesised by Windaus and Vogt (*Ber.*, 1907, **40**, 3691) from  $\beta$ -glyoxaline-4(or 5)-propionic acid by Curtius's method. More recently, Ackermann (*Zeitsch. physiol. Chem.*, 1910, **55**, 504) has succeeded in obtaining a relatively large yield of the base by the putrefaction of histidine.

Neither method is very satisfactory, since the first is somewhat complex and expensive, while the yields are by no means good. The second method is wholly uncertain in its results. The object

of our investigation was therefore to endeavour to find a simple method of obtaining the base directly from histidine, which is comparatively easily obtainable. In this we were only partly successful, since we were able to obtain only moderate yields of the base by the action of acids in sealed tubes at a temperature of from 265° to 270°. This last factor (temperature) made it a matter of very great difficulty to obtain anything like large amounts of the base. The results obtained, however, were deemed of sufficient interest to form the subject of the present communication.

Experiments were first carried out to determine whether, as in the case of the formation of *p*-hydroxyphenylethylamine from tyrosine, carbon dioxide could be removed from histidine by direct heating. It was found, however, that under varying conditions only a very small amount (0·3 to 1·0 per cent.) of base could be obtained, and the method was abandoned.

By directly heating the monobenzoyl derivative of histidine and subsequently hydrolysing, a somewhat better yield (10 to 20 per cent.) of the base was obtained.

The effect of various acids under varying conditions of temperature and concentration was then investigated, and it was found that yields of base amounting to about 25 per cent. of the theoretical could be obtained with concentrated hydrochloric acid, moderately dilute sulphuric acid, and fused potassium hydrogen sulphate under suitable conditions. After heating for three hours with acids at temperatures below 240°, no formation of 4(or 5)- $\beta$ -aminoethylglyoxaline took place. At about 240° very little of the base was obtained, the main product of the reaction being *r*-histidine, which had previously been prepared by Fränkel (*Beitr. Chem. Physiol. Path.*, 1906, **8**, 156) in a similar manner. As the temperature was raised, the yield of base gradually improved, and reached a maximum (about 25 per cent. of the theoretical) at about 265–270°. Further increase of temperature led to diminished yield of 4(or 5)- $\beta$ -aminoethylglyoxaline. With phosphoric acid (14 per cent.) at 250°, no base was produced, nor did the use of hydrogen bromide in acetic acid solution at somewhat lower temperatures yield any better results.

The progress of the work was very greatly facilitated by the physiological estimation of the yield of base in many of our experiments. This was kindly undertaken for us by Dr. H. H. Dale and Dr. P. P. Laidlaw, to whom we wish to express our indebtedness and thanks.

During the course of the investigation some hitherto undescribed salts of histidine and 4(or 5)- $\beta$ -aminoethylglyoxaline were prepared, and are now described.

### EXPERIMENTAL.

#### *The Action of Concentrated Hydrochloric Acid on Histidine.*

One gram of histidine hydrochloride was heated in a sealed tube with 2 c.c. of concentrated hydrochloric acid to 270° for three hours. The solution was concentrated and neutralised. To the boiling solution was added an excess of solid picric acid. On cooling, a crystalline precipitate separated, which was collected and freed from picric acid by extraction with ether. The residue, when recrystallised from water, gave 0·2 gram of 4(or 5)- $\beta$ -aminoethylglyoxaline dipicrate, melting at 233—235°.

#### *The Action of Dilute Sulphuric Acid.*

(a) At 265—270°.—Two grams of histidine monohydrochloride were heated in a sealed tube to 265—270° for three hours with 1 c.c. of a 20 per cent. aqueous solution of sulphuric acid. The reaction product (a dark brown liquid) was treated with sodium carbonate solution until no further precipitate separated, filtered, and the filtrate neutralised and concentrated to about 15 c.c. An equal volume of cold saturated aqueous solution of picric acid was added, and the amorphous precipitate quickly collected. To the filtrate was added 1·5 grams of picric acid in hot saturated aqueous solution. A little resinous precipitate was removed from the hot solution, and the crystalline precipitate, which separated on cooling, was recrystallised from hot water. There was thus obtained 0·85 gram of a picrate (m. p. 228—229°), which crystallised in bunched, slightly curved, pointed needles. Repeated recrystallisation did not raise the melting point above 233—234°, and analysis showed the salt to be the hitherto undescribed 4(or 5)- $\beta$ -aminoethylglyoxaline monopicrate:

0·0978 gave 0·1396 CO<sub>2</sub> and 0·0282 H<sub>2</sub>O. C=38·8; H=3·2.

C<sub>11</sub>H<sub>12</sub>O<sub>7</sub>N<sub>6</sub> requires C=38·8; H=3·5 per cent.

The monopicrate, on recrystallisation from a large excess of picric acid solution, readily yielded the dipicrate corresponding in all respects with that described by Windaus and Vogt (*loc. cit.*).

#### *4(or 5)- $\beta$ -Aminoethylglyoxaline Dihydrobromide.*

The dihydrobromide was prepared by thoroughly shaking the finely powdered dipicrate with ether and a slight excess of dilute hydrobromic acid until all the dipicrate had disappeared. The aqueous solution of the hydrobromide thus obtained was then freed from picric acid by means of ether, digested with a little animal charcoal, filtered, and evaporated to dryness in a vacuum. The

residual brown gum became crystalline on the addition of absolute alcohol, and the salt was then purified by recrystallisation from this solvent.

The salt forms stout, colourless, prismatic needles, which melt to a brown liquid at 284° (corr.), after gradually darkening and sintering from about 265°. It is very readily soluble in water, but sparingly so in boiling absolute alcohol. It is anhydrous:

0·1200 gave 0·0957 CO<sub>2</sub> and 0·0440 H<sub>2</sub>O. C=21·7; H=4·1.

C<sub>5</sub>H<sub>9</sub>N<sub>3</sub>.2HBr requires C=22·0; H=4·1 per cent.

(b) At 240—250°.—Seventy grams of histidine monohydrochloride were heated in sealed tubes with 140 c.c. of 20 per cent. sulphuric acid for three hours at 240—250° in quantities of not more than 4 grams of histidine in one tube; even under these conditions tubes representing 23 grams exploded. The reaction product from the remaining tubes was worked up exactly as described above. There was thus obtained 26·7 grams of a picrate, which melted at 180—190°. On extracting with absolute alcohol, the greater portion dissolved, and the sparingly soluble residue, after recrystallisation from water, gave 4·3 grams of 4(or 5)-β-aminoethylglyoxaline dipicrate. The alcoholic extract was evaporated and the residue, on crystallisation from water, gave 16·6 grams of pure *r*-histidine dipicrate.

*r-Histidine dipicrate* crystallises from water in thin, yellow plates, which contain two molecules of water. After drying at 100°, it begins to sinter at 182°, and decomposes at 190° (corr.). It is readily soluble in alcohol or hot water, but sparingly so in cold water:

0·1660 \* lost 0·0091 at 100°. H<sub>2</sub>O=5·5.

C<sub>18</sub>H<sub>15</sub>O<sub>16</sub>N<sub>9</sub>.2H<sub>2</sub>O requires H<sub>2</sub>O=5·5 per cent.

0·1468 † gave 0·1906 CO<sub>2</sub> and 0·0356 H<sub>2</sub>O. C=35·4; H=2·7.

0·1364 † „ 24·0 c.c. N<sub>2</sub> at 23° and 766 mm. N=20·5.

C<sub>18</sub>H<sub>15</sub>O<sub>16</sub>N<sub>9</sub> requires C=35·2; H=2·5; N=20·6 per cent.

This salt readily gave the dihydrochloride, which sinters and melts at 225° (corr.); Fränkel (*loc cit.*) gives 220°.

*r-Histidine sesquihydrochloride*, (C<sub>6</sub>H<sub>9</sub>O<sub>2</sub>N<sub>3</sub>)<sub>2</sub>·3HCl·H<sub>2</sub>O, crystallises in clusters of flat, prismatic needles when the dihydrochloride is crystallised from dilute alcohol (for instance, when it is dissolved in about twice its weight of water, and four times its weight of alcohol is added). This salt melts at 168—170° (corr.), and suffers no loss in weight at 100°:

0·1513 gave 0·1840 CO<sub>2</sub> and 0·0734 H<sub>2</sub>O. C=33·2; H=5·4

0·1270 „ 0·1530 CO<sub>2</sub> „ 0·0644 H<sub>2</sub>O. C=32·9; H=5·7.

\* Air-dried salt.

† Dried at 100°.

0·1570 gave 0·1555 AgCl. Cl=24·5.

0·1259 „ 0·1251 AgCl. Cl=24·6.

$(C_6H_9O_2N_3)_2 \cdot 3HCl \cdot H_2O$  requires C=32·9; H=5·3;  
Cl=24·3 per cent.

The composition of this salt is peculiar; there is no evidence of a similar salt of the natural histidine (compare Abderhalden and Einbeck, *Zeitsch. physiol. Chem.*, 1909, **62**, 322).

*L-Histidine monopicrate* crystallises from water in large, flat plates which are sparingly soluble in hot water and almost insoluble in alcohol. This salt decomposes at 180°–181° (corr.), after sintering from about 175°. It contains one molecule of water of crystallisation:

0·3983 \* lost 0·0185 at 110°.  $H_2O=4\cdot6$

$C_{12}H_{12}O_9N_6 \cdot H_2O$  requires  $H_2O=4\cdot5$  per cent.

0·1825 † gave 0·2515 CO<sub>2</sub> and 0·0531 H<sub>2</sub>O. C=37·6; H=3·3.

$C_{12}H_{12}O_9N_6$  requires C=37·5; H=3·2 per cent.

When this salt is dissolved in a hot aqueous solution of picric acid, the dipicrate (m. p. 190°) separates on cooling.

For purposes of comparison, attempts were made to prepare a mono- and di-picrate of naturally occurring histidine. Histidine appears, however, to form only a dipicrate.

*Histidine dipicrate* crystallises from water in long, flat, clear, well-formed leaflets, which sinter at about 80° and melt at 86° (corr.). It appears to contain two molecules of water:

0·1591 \* gave 0·1927 CO<sub>2</sub> and 0·0452 H<sub>2</sub>O. C=33·0; H=3·2.

$C_{15}H_{16}O_9N_6 \cdot 2H_2O$  requires C=33·3; H=3·0 per cent.

#### *The Action of Potassium Hydrogen Sulphate on Histidine.*

Twenty-five grams of potassium hydrogen sulphate were fused in a beaker heated by an oil-bath and 1 gram of histidine monohydrochloride was added; considerable frothing occurred, and the mixture had to be stirred frequently. After heating for various lengths of time at different temperatures, the reaction product was dissolved in water, neutralised with potassium hydroxide, digested with animal charcoal, cooled, and filtered from charcoal and potassium sulphate. The filtrate was again concentrated, separated from more potassium sulphate, made up to a known volume, and the yield of 4(or 5)- $\beta$ -aminoethylglyoxaline determined physiologically. Heating at an oil-bath temperature of 260°–270° for one hour gave the best yield of the desired base, but the maximum only reached about 5 per cent. of the theoretical. A modification of this method, in which histidine monohydrochloride was heated with ten times its

\* Air-dried salt.

† Dried at 110°.

weight of potassium hydrogen sulphate in sealed tubes at 235–270° for three hours, gave yields of 20 to 25 per cent. of the theoretical, as indicated by physiological estimation.

*The Formation of 4(or 5)- $\beta$ -Aminoethylglyoxaline from Benzoylhistidine.*

Monobenzoylhystidine was prepared by the Schotten-Baumann method, as indicated by Fränkel (*loc. cit.*). It was, however, found to be quite unnecessary to carry out the precipitation with mercuric chloride described by him. On neutralising the solution after the reaction is complete, the pure benzoyl derivative separates very quickly on simply keeping.

One gram of benzoylhystidine so obtained was heated in a vacuum at 240° until all frothing ceased. The black, tarry mass was dissolved in 2 c.c. of concentrated hydrochloric acid, and hydrolysed at 180°. The contents of the tube were washed out with water, and the separated benzoic acid collected, the filtrate extracted with ether, and the aqueous solution neutralised. An equal volume of a solution of picrolonic acid in water was added, and the bulky, amorphous, yellow precipitate collected. The filtrate was concentrated to small bulk, and a concentrated alcoholic solution of picrolonic acid added. After some time, 0·47 gram of 4(or 5)- $\beta$ -aminoethylglyoxaline picrolonate was obtained, crystallising in bunches of needles, and melting at 262–264° (Windaus and Vogt, *loc. cit.*, give "about 266°").

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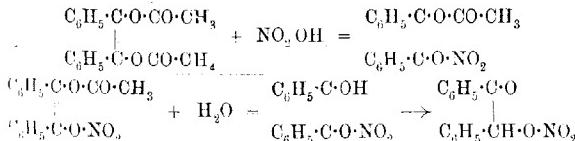
XLIV.—*The Nitration of Acetylbenzoin and of  
Stilbenediol Diacetates.*

By ARTHUR GORDON FRANCIS and CHARLES ALEXANDER KEANE.

THE object of this investigation has been to obtain some unsymmetrical derivatives of benzoin, such as the nitro-compounds, with the view of examining their stereochemical and desmotropic relations. The action of nitric acid on benzoin and some allied compounds offers several points of interest. Benzoin itself, as is well known, is oxidised to benzil when heated with ordinary concentrated nitric acid, but with fuming nitric acid at 0° *p*-nitrobenzil is also obtained.

Benzil is less readily nitrated; on heating it with fuming nitric acid two nitro-groups are introduced to form two isomeric dinitro-compounds, melting respectively at 131° and 147° (Zagumenny, *J. Russ. Phys. Chem. Soc.*, 1873, **4**, 278); mononitrobenzils have not been obtained directly from benzil. The action of nitric acid on acetyl- and on benzoyl-benzoin has been studied by Zinin (*Annalen*, 1857, **104**, 116). From acetylbenzoin he obtained a mixture of two nitro-compounds, neither of which, however, appears to have been isolated in a pure state or submitted to more than a preliminary investigation. The nitrobenzoyl compound he obtained pure, and isolated it in rhombic tablets, melting at 137°.

With the object of preparing nitrobenzoin, attempts were first made to hydrolyse nitrobenzoylbenzoin, but it was not found possible to effect this decomposition with any hydrolytic agents, as complex condensation products, which are still under investigation, invariably resulted. In order to obtain a less stable ester, *p*-nitroacetylbenzoin was prepared, but condensation products were similarly formed on hydrolysis, and all attempts to obtain *p*-nitrobenzoin by the action of hydrolytic agents from it were unsuccessful. Attention was then directed to the nitration of the geometrically isomeric stilbenediol diacetates prepared by Thiele (*Annalen*, 1899, **306**, 142). These compounds are so readily hydrolysed to benzoin that it appeared probable that by effecting the nitration in absence of hydrolytic agents, nitro-compounds of the diacetyl isomerides might be obtained, from which nitrobenzoin could be prepared. The experiments conducted with this object in view resulted in the formation of benzoin mononitrate and a small quantity of a substance, possibly nitrobenzoin, which is still under examination, together with benzil. Both the  $\alpha$ -stilbenediol diacetate melting at 153° and the  $\beta$ -compound melting at 110° act similarly towards nitric acid, except for the fact that the isomeride of lower melting point is partly converted into the  $\alpha$ -compound under the conditions described below. The action of nitric acid may be represented by the following equations, the final formation of benzoin nitrate being due to a molecular rearrangement, as in the preparation of benzoin from the stilbenediol diacetates:



This difference in the behaviour of acetylbenzoin, benzoylbenzoin,

and of the stilbenediol diacetates towards nitric acid is shared by several other reagents, and similar differences have also been observed with some of their derivatives. These reactions are under further investigation.

#### EXPERIMENTAL.

##### *Nitration of Acetylbenzoin.*

Zinin (*Annalen*, 1857, **104**, 120), Jena and Limprecht (*ibid.*, 1870, **155**, 92), and Päpcke (*Ber.*, 1888, **21**, 1336) have all prepared acetylbenzoin, but give different melting points for the compound, namely, below 100°, 75°, and 83° respectively. It is best prepared as follows: 200 grams of benzoin are added in successive small quantities to a mixture of 25 c.c. of concentrated sulphuric acid and 500 c.c. of acetic anhydride kept cold in running water; the mixture is kept for some time, poured into water, the precipitate collected, and recrystallised from 90 per cent. alcohol. The product thus prepared melts at 83°, agreeing with the value given by Päpcke. A practically quantitative yield is obtained by this method of preparation.

Two methods of nitration were employed.

*Method I.*—For the nitration by this method, 400 grams of fuming nitric acid are cooled to 0° in a freezing mixture of ice and salt, and 200 grams of finely powdered acetylbenzoin gradually added. The acetyl compound must be thoroughly dry, free from odour of acetic acid, and finely powdered, and the temperature must be kept within a degree or so of 0°; if it falls much below this temperature, considerable quantities of benzoin are formed, and above this temperature the amount of benzil formed is increased. The deep red solution thus obtained is poured at once into ice-cold water, when a pale green oil separates, which is well washed by decantation with water. After some time this sets to a semi-solid mass, from which the nitro-compound is separated by treatment with successive small quantities of ether, whereby the adherent oil is removed. The residue is recrystallised from 90 per cent. alcohol. A yield of 20 per cent. on the weight of acetylbenzoin taken is obtained.

*Method II.*—Five grams of acetylbenzoin are treated with 25 c.c. of acetic anhydride, 4 c.c. of concentrated sulphuric acid, and 17 grams of recently fused and finely powdered nitre at a temperature of -15°. The nitration is carried out as in the case of the stilbenediol diacetates described below. A yield of 40 per cent. on the weight of the acetylbenzoin taken is obtained.

p-Nitroacetylbenzoin crystallises from 90 per cent. alcohol in brilliant, almost colourless leaflets, and melts at 125° (uncorr.). It

is sparingly soluble in ether or light petroleum, readily so in chloroform, acetone, or benzene, and somewhat less so in boiling 90 per cent. alcohol or glacial acetic acid. It is decomposed by alkalis in either aqueous or alcoholic solution, with the formation of acidic condensation products, as stated above:

0·2064 gave 0·4846 CO<sub>2</sub> and 0·0834 H<sub>2</sub>O. C=64·03; H=4·83.

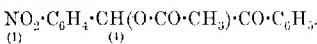
0·5640, 24·0 c.c. N<sub>2</sub> (moist) at 20° and 755 mm. N=4·83.

0·7421, in 20 c.c. alcohol, gave E=0·19°. M.W.=305.

C<sub>16</sub>H<sub>13</sub>O<sub>3</sub>N requires C=64·20; H=4·35; N=4·68 per cent.  
M.W.=299.

When heated with nitric acid (D 1·40), *p*-nitrobenzil, melting at 140°, is formed. (Found, N=5·34. Calc., N=5·49 per cent.)

When oxidised with a mixture of sulphuric acid (25 grams of concentrated sulphuric acid in 25 c.c. of water) and an approximately normal solution of potassium dichromate, it is completely hydrolysed and oxidised to acetic acid, benzoic acid (melting at 122°), and *p*-nitrobenzoic acid (melting at 237°). Care must be taken to have always an excess of dichromate present during the oxidation, otherwise acidic condensation products result. Benzoin, under precisely the same conditions, yields molecular proportions of benzaldehyde and benzoic acid. From this it follows that the nitro-group is in the para-position in the phenyl radicle connected with the carbon atom of the secondary alcohol group, so that the nitroacetylbenzoin has the structural formula:



The identity of the *p*-nitrobenzoic acid formed in the oxidation was confirmed by titration with alkali. (Found, M.W.=166·4. Calc., M.W.=167.)

*Nitration of the Stilbenediol Diacetates ( $\alpha$ , melting at 153°, and  $\beta$ , melting at 110°).*

Forty c.c. of concentrated sulphuric acid are added, drop by drop, to 250 c.c. of acetic anhydride kept cold in a freezing mixture of ice and salt; when the temperature has fallen to -15°, 45 grams of the finely powdered  $\beta$ -stilbenediol diacetate (melting at 110°) are added, and then 17 grams of recently fused and finely powdered nitre in small portions at a time and with constant shaking, care being taken to keep the temperature at -15°. If the diacetate be added to the mixed acid, anhydride, and nitre, no benzoin nitrate is formed. When all the nitre has been added, the solution, which is clear and red in colour, is poured into the bath liquor, cooled to -15°, and the whole stirred until solid. The supernatant acid liquid is then decanted, the residue being thoroughly washed by

decantation, and collected. The bulk of the benzil present is removed by washing with ether, and the residue purified by fractional crystallisation from 90 per cent. alcohol. The products isolated consisted of: (1) benzoin mononitrate, melting at 167°, 3 grams;  $\alpha$ -stilbenediol diacetate, melting at 153°, 3 grams; and the substance, melting at 188°, 1 gram.

The amount of  $\alpha$ -stilbenediol diacetate formed increases with decrease of temperature; at 0°, 5 per cent. of the  $\beta$ -diacetate used is obtained, at -15°, 7 per cent., at -25°, 10 per cent., whilst no benzoin nitrate is formed either at 0° or at -25°.

The  $\alpha$  diacetate, melting at 153°, gives a somewhat better yield of benzoin nitrate, 25 grams yielding 2 grams of benzoin nitrate, melting at 167°, and 2 grams of unchanged  $\alpha$  diacetate, melting at 153°. None of the  $\beta$ -isomeride is formed in the reaction.

*Benzoin mononitrate* crystallises from 90 per cent. alcohol in beautiful, colourless plates, and melts at 167° (uncorr.). It is very sparingly soluble in ether, light petroleum, or cold 90 per cent. alcohol, but dissolves fairly readily in boiling 90 per cent. alcohol. On hydrolysis with potassium hydroxide, it yields benzoin and potassium nitrate, and on heating with concentrated nitric acid it gives benzil. The complete combustion of the nitrate is exceedingly difficult, as it burns explosively; the analytical results, however, leave no doubt as to the composition of the compound:

0·1461 gave 0·3482 CO<sub>2</sub> and 0·0732 H<sub>2</sub>O. C=65·0; H=5·56.

0·1891 " 8·70 c.c. N<sub>2</sub> (moist) at 15° and 762 mm. N=5·41.

0·2090 " 9·25 c.c. N<sub>2</sub> " 14° " 763 mm. N=5·23.

0·4838, in 20 c.c. alcohol, gave E=0·16°. M.W.=238.

C<sub>14</sub>H<sub>11</sub>O<sub>4</sub>N requires C=65·37; H=4·28; N=5·45 per cent.  
M.W.=257.

The substance melting at 188° is very sparingly soluble in 90 per cent. alcohol, but can be obtained crystalline from this solvent in fine, light yellow needles. It is unchanged by boiling with potassium hydroxide, and is therefore not a nitrate; its composition corresponds with that of nitrobenzoin:

0·3482 gave 16·4 c.c. N<sub>2</sub> (moist) at 13° and 760 mm. N=5·57.

C<sub>14</sub>H<sub>11</sub>O<sub>4</sub>N requires N=5·45 per cent.

CHEMISTRY DEPARTMENT,  
THE SIR JOHN CASS TECHNICAL INSTITUTE,  
ALDGATE, E.C.

XLV.—*Studies of the Processes Operative in Solutions.*  
*Part XII.\* The Apparent Hydration Values of*  
*the Acid Systems and of Salts deduced from a*  
*Study of the Hydrolytic Activities of Acids.*

By FREDERICK PALLISER WORLEY, M.A., M.Sc., New Zealand,  
Leathersellers' Company's Research Fellow, City and Guilds of  
London Institute, Central Technical College.

THE first communication of this series was an account of experiments made with the object of studying the influence of various "neutral" substances, both electrolytes and non-electrolytes, on the siccoclastic activity of chlorhydric acid; in the third, similar experiments with nitric acid were described; in the seventh, the relative activities of the two acids and of sulphuric acid were compared from several points of view; in the eighth, the nature of the influence on the hydrolytic activity of acids exercised by salts was considered more broadly than in previous communications, especially with reference to the peculiarities apparent in the case of weak hydrolytes.

The present communication is an account of a closer and more complete study of the behaviour of cane sugar in aqueous solutions towards chlorhydric and nitric acids and of the influence of salts on the rate of change than was possible heretofore with the appliances at disposal; although undertaken with the object of obtaining the data for a full discussion of the processes operative in hydrolytic changes, it has afforded results that render the careful consideration desirable of the extent to which the polarimetric method may be used as a method of following the course of a chemical change. It was felt that the experimental difficulties attending such an inquiry had not all been overcome—particularly that it was necessary to secure more complete control over the

\* The previous parts of these studies (I—XI) are published in the Proceedings of the Royal Society, A, 1906, 78; 1907, 79; 1908, 81; 1910, 84. A summary of the work is given in No. XIX. (*Chem. News*, 1911, 103, 97). Attention may be called to certain departures from the conventional nomenclature adopted in the communications. The compound represented by the formula HCl is termed hydrogen chloride, not hydrochloric acid, for reasons advocated by me as far back as 1885 in my address to the Chemical Section of the British Association in Aberdeen; the acid that is formed when hydrogen chloride and water associate is spoken of as chlorhydric acid. In like manner, the compound formulated as HO<sup>+</sup>NO<sub>2</sub> is spoken of as hydrie nitrate, the solution of this compound in water being alone spoken of as nitric acid. The object in view in adopting this course will be discussed in a later communication.—HENRY E. ARMSTRONG.

temperature conditions—and that if the refinements of which an account has been given previously (IX) were introduced the errors would at least be reduced to a minimum, so that it would be possible, with a close approach to certainty, to determine the direction in which departures from constancy took place as the action progressed or when the conditions were varied.

In previous work, cane sugar has been used as the hydrolyte in order to ascertain the effect produced by various substances on the course of change; the inquiry was undertaken in the hope that evidence would be obtained as to the state of the substances in solution.

The changes undergone by the sugar and their possible influence on the course of change have scarcely been taken into consideration hitherto. It has always been assumed tacitly that the resolution of the sugar molecule into the two hexose molecules is without influence on the result but it is difficult to believe that this is the case, as the increase in the number of molecules in solution must affect the "osmotic" conditions and must give rise to disturbances of some magnitude: if such changes be not apparent in the result, it must be because compensating influences are at work which mask their effect.

Again it is customary to suppose that it is unnecessary to take into account the water which disappears as hydrolysis proceeds—on the ground that this forms only a small proportion of the total amount present; it appeared to be desirable to ascertain the limits within which this argument held good and within which the observations might be reduced on the assumption that only a single changing substance is to be considered.

#### *Determination of the End-point in the case of Concentrated Solutions.*

It has been customary to follow the course of change with the polarimeter, observing the rotatory power of the solution at known intervals of time, a final observation being made to determine the "end-point" when the change is judged to be complete. This determination is of primary importance: if the end-point be determined incorrectly, it is impossible to deduce a correct value of  $K$  in the mass-action equation:

$$K = \frac{1}{t} \log \frac{a}{a-x}.$$

At an early stage of the inquiry, doubt arose as to the propriety of the method usually adopted. When observations were carried on during a considerable period, the disquieting fact was disclosed that

the action did not come to an end. Thus, in an experiment with one molecular proportion of cane sugar, one of hydrogen chloride and forty of water, the solutions were mixed at 10.35 a.m. on a Friday and readings were taken at intervals until 9.15 a.m. on the following day: by four o'clock on Friday afternoon, the rotatory power had fallen to 161°34° (the zero being approximately 180°); at five o'clock it was 161°22°; from six until eight it was constant at 161°20°; it then began to rise, the readings being 161°21° at 9 p.m., 161°25° at 12.30 a.m., 161°28° at 3 a.m., 161°30° at 6.30 a.m., 161°33° at 9.15 a.m. Under the usual conditions, the final reading would not have been taken probably until several hours later, when the rotatory power would have risen still further.

Even in the case of much more dilute solutions, the rise is easily detected. In an experiment made with only a quarter as much sugar as in that above quoted, the solutions were mixed at 10.20 a.m. on Friday: at 2.30 p.m. the reading was 174°86°, at 3.30 p.m. 174°66°, at 5.30 p.m. and at 6.10 p.m. it lay between 174°65° and 174°66°; by noon the next day, it had risen to 174°67° and by 3.45 p.m. on Monday to 174°74°.

Although, in the case of dilute solutions, the change in the "end-point" is often so small as to be negligible, in the case of relatively concentrated solutions it cannot be neglected. Apparently the rise is due to a change affecting one or both of the primary products of hydrolysis. It is to be supposed that this change sets in as soon as the hydrolysis begins and that it continues at an increasing rate as the hexoses increase in amount, reaching a maximum towards the close of the period of hydrolysis.

The apparently constant minimum is reached when the change in the rotatory power due to the hydrolysis becomes as small as that due to the secondary change; it is not the minimum that would have been obtained in the absence of secondary change but a higher value. Moreover, when the end-point is deduced in the usual way from a single observation about twenty-four hours from the commencement of the experiment, probably the minimum has been passed and the rotatory power has increased, thus introducing a still greater error.

The question arises whether this change (which sets in at the beginning of the experiment) affects readings other than those of the end-point? In point of fact, there can be little doubt that its effect is so small at the beginning of the hydrolysis as to be negligible. To determine the rate at which the primary change occurs, however, it is necessary to eliminate the effect of the secondary change by finding the end-point that would have been reached if the primary change alone had occurred.

It is impossible to deduce a "theoretical" end-point, both on account of the effect of the catalyst on the rotatory power of the cane sugar and of the hexoses into which it is converted and on account of the effect that the various optically active substances exercise reciprocally on their individual rotatory powers. The preparation of solutions containing the two hexoses and the acid catalyst with the required amount of water such as should remain at the close of the experiments, if not out of the question, would be difficult on account of the trouble and errors involved in this procedure.

Fortunately it is possible to correct for the secondary change in each experiment by determining the rate at which the change is taking place. For this purpose, after the rise becomes regular, readings are taken at intervals of from eight to twenty-four hours. The total effect of the secondary change is then found by assuming that it has continued at this rate from the time when half the sugar has been inverted. It is believed that this method affords a very close approximation to the truth. The result is most conveniently arrived at graphically.

By proceeding in this manner, the "corrected" end-point deduced in the case of the example quoted was 161.11°, whereas that observed directly in the ordinary way would have been about 161.4°.

#### *Evaluation of K.*

The formula usually adopted,

$$K = \frac{1}{t} \log_a \frac{a}{a-x}$$

necessitates an initial reading giving the value  $a$  at any arbitrary time  $t_0$  and a subsequent series of readings giving a series of values of  $a-x$  after times  $t_1, t_2, t_3$ , etc. It is obvious that any error in the initial value affects all the values of  $K$  and also that as  $t$  increases observational errors are gradually obscured. On this account, a comparatively even set of values of  $K$  may be deduced from tolerably inaccurate observations. There is the additional disadvantage that any real divergence from constancy in the value of  $K$  will tend to be obscured. The difficulties are overcome by using the formula in the slightly different form:

$$K \text{loge} = \frac{1}{t_2 - t_1} \log_{10} \frac{a - x_1}{a - x_2}$$

deducing values of  $K$  for equal intervals of time.

To obtain values of  $K$  of convenient magnitude,  $K \text{loge}$  is multiplied by  $10^5$ . The values of  $K$  given in subsequent tables are always those of  $K \text{loge} \times 10^5$ , the unit of time being 1 minute.

In this way any error common to the series, due to an error in

the initial reading, is obviated; moreover, by making the interval of time as small as the accuracy of the observations will allow, the change in the value of  $K$  due to a departure from the unimolecular law becomes more obvious. If the interval of time is small, the sugar will be the only variable during the interval, the change in the water being negligible. It is legitimate therefore under such conditions to treat the interaction as unimolecular; any departure from the law will be shown by differences in the values of  $K$  at different periods, as changes in other factors than the sugar become significant.

The values of  $K$  found by means of the above formula, using the corrected end-points, show a marked regular rise as hydrolysis proceeds; previous observers appear to have overlooked this change.

The following example may be quoted in illustration. The experiment was one in which one molecular proportion of hydric nitrate and one of sugar were dissolved in sixty molecular proportions of water.

TABLE I.

Time from mixing in minutes	15	20	25	30	35	40	45	50	55	75	95
$K$ .....	425.8	427.6	428.0	428.7	430.5	430.9	431.6	431.8	432.5	435.7	

The values of  $K$  are shown by this example—only one of the many that might be quoted—to be inconstant. In less concentrated solutions the rise in the value of  $K$  is not so great but becomes imperceptible only in very dilute solutions.

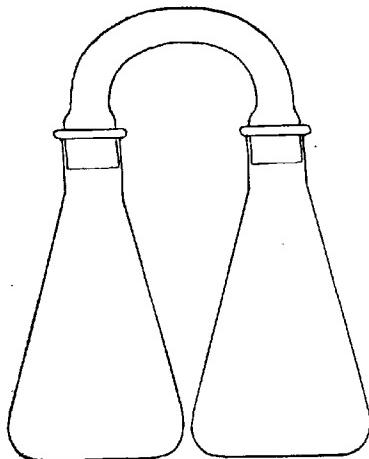
The method ordinarily adopted, by which the ultimate value of  $K$  is taken to be the mean of the various separate values, is clearly one which cannot be followed legitimately except in the case of dilute solutions: each separate value of  $K$  corresponds presumably with some particular condition of the solution in which changes are proceeding.

If the rates of hydrolysis in different experiments under different conditions are to be compared, it is essential that the value of  $K$  corresponding with some particular condition should be determined: from this point of view, the value at the very commencement of the interaction is obviously that which it is most desirable to determine. It is arrived at in the following way.

The solutions of sugar and of acid are prepared and mixed in the apparatus shown in Fig. 1. This consists of two 100 c.c. Jena flasks connected by a bent tube, of wide bore, the ends of which are carefully ground to fit into the necks of the flasks. The acid is weighed into one flask and sugar into the other together with the amount of water necessary to effect the degree of dilution desired. The solutions can be kept unmixed in such an apparatus until required

and then heated to the temperature at which the experiment is to be made and thoroughly mixed at that temperature without risk of loss by evaporation. The mixture is quickly transferred to the polarimeter tube and readings are taken as soon as the temperature is deemed to be constant. Values of  $K$  are then determined 15, 20, 25, 30, etc., minutes after mixing, the time interval  $t_2 - t_1$  being made as short as the observational error will allow. From these values, the value of  $K$  at the time 0 is found by extrapolation. Very great care and practice are required to secure sufficiently regular values; it is only when every attention is paid to the

FIG. 1.



adjustment of the temperature and to all recognisable sources of error that really trustworthy results are secured.

The value of  $K$  thus determined is independent of the other changes going on in the solution. It is a measure of the rate of inversion, under definite known conditions of concentration of sugar, acid and water, at the commencement of the period of change when the products of change are without influence. This value alone will be given throughout this communication.

In the case of the example quoted above, the value at the time of mixing found by extrapolation was slightly below 424. The method generally used does not involve particular care being taken to obtain observations immediately after mixing but an interval,

perhaps thirty minutes, is allowed to lapse before the initial reading is taken; consequently, the values of  $K$  found by the ordinary method are those at times beginning more than forty minutes after mixing and continuing later than in the case of the above example; the values of  $K$  deduced by the method would lie somewhere between 430 and say 438, giving a mean very different from the initial value arrived at by the method advocated in the previous section, namely, 424. In more concentrated solutions than that referred to, the rate of alteration of the end-point would be greater and the increase in the value of  $K$  greater, thus introducing the possibility of still larger errors.

In this connexion, it is necessary again to emphasise the extreme importance of a correct determination of the end-point, as a small alteration in its value causes a large alteration in each value of  $K$ . Moreover, by slightly raising the end-point, the values of  $K$  are raised, the later to a greater extent than the earlier; lowering the end-point has the effect of reducing the value of  $K$ , the later values being those most affected. It is therefore obvious that in a case in which the values of  $K$  should actually be of constant magnitude, they may appear to rise or fall if the end-point determined be too high or too low.

Before the method of correcting the end-point by extrapolation had been devised, acting under the belief that has been accepted hitherto that a constant may be obtained by applying the unimolecular equation, attempts were made to deduce constant values of  $K$  by taking some value lower than that observed, which was obviously too high in many cases. It was found that if the observed values were but slightly adjusted,  $K$  could be made practically constant, varying in some cases less than a single unit, over a considerable range, in a constant of 800. When, however, the corrected end-point was deduced in the manner explained above, it was evident that the adjustment required to make  $K$  constant was not in correspondence with the observed rate of rise due to the secondary change but considerably greater. Moreover, when the change was followed over a greater part of its course than is customary, by adjusting the end-points constant values of  $K$  could be deduced only during the middle period—the period during which it has been customary to make the observations—thus emphasising the danger of making deductions from the study of an interaction over a narrow range.

It is more than probable that in the past "constant" values have not infrequently been arrived at because the impression has prevailed that the values should be constant and departures from uniformity have been interpreted as experimental errors.

It remains to point out that the method advocated is applicable only to the earlier periods of change during which the magnitude of the effect produced by the secondary changes is negligible. It is unfortunate that this is the case, as several of the issues to be decided cannot be discussed satisfactorily without the knowledge of the course taken by the change throughout the entire period.

#### *Nature of the Interaction.*

The rise in the values of  $K$  in the example given in table I cannot be attributed to the alterations made in the observed end-point, as the corrections introduced have involved the lowering of the observed end-point: consequently the later values of  $K$  are reduced to a greater extent than the earlier values—in other words, if no alterations had been made in the end-points, the rise in the values of  $K$  would have been still greater.

A question now to be considered is whether the increase in value of  $K$  cannot be explained by the change in the active mass of the water. It has always been assumed that the hydrolysis of cane sugar is a bimolecular change in which sugar and water both take part and that when the change in the concentration of the water becomes significant the rate of hydrolysis is expressed by the equation:

$$\frac{dx}{dt} = K'(a - x)(b - x),$$

( $b - x$ ) representing the active mass of water.

In any experiment, the several values of  $K$  deduced from the unimolecular equation:

$$\frac{dx}{dt} = K(a - x) \text{ are those of the ratio } \frac{dx}{\frac{dt}{a - x}}.$$

In the bimolecular equation, this ratio is equal to  $K'(b - x)$ :  $K'$  being by hypothesis constant throughout the experiment.  $K'(b - x)$  must decrease as the water is used up during hydrolysis. In point of fact, instead of diminishing, it increases: plainly, showing that taking into account the change of active mass of the water would merely accentuate the want of constancy: in other words, the hydrolysis of cane sugar by acids cannot be treated as a simple case of bimolecular change in which merely water and sugar are the interacting substances.

Besides the reduction in the active mass of the water, other important changes take place as hydrolysis proceeds. In place of each molecule of cane sugar, two hexose molecules come into existence; changes also take place in the degree of association of the

various substances present in the solution; the ratio of acid to water also increases as water is used up; lastly, it is well known that although the rotatory power of cane sugar and of dextrose is but slightly affected by changes of concentration, that of lævulose is subject to considerable change. The changes in optical activity to be considered, however, are not merely those which the various substances undergo in simple solutions; the task is the far more difficult one of taking into account the changes which take place under the reciprocal influence of the various substances in solution—of the acids as well as of the various sugars.

The alteration in the value of  $K$  as the interaction proceeds is undoubtedly the algebraic sum of all such influences as have been referred to. It is improbable that the separate effect of each of the influences pictured can be evaluated. It cannot be too clearly emphasised, therefore, that no positive deduction can be made from the fact that  $K$  either remains constant or alters in value during the course of an experiment—on account of the numerous secondary influences, which increase in magnitude as the change proceeds.

Moreover, if the influences referred to either detract from or increase the optical rotatory power of the solutions, it cannot be asserted that the optical change affords a true measure of the course of chemical change: if the rate of change in optical characters be not strictly proportional to the rate at which the chemical change proceeds, it is obvious that the results arrived at are not those sought for and do not afford a strict measure of the rate of chemical change.

Whilst therefore the initial values of  $K$  determined by the optical method under different conditions may be used in comparing the changes which set in under these different conditions, it would seem that the method is of less value in studying the changes which the sugar itself undergoes under any particular set of conditions in an individual experiment.

Although by far the most accurate as well as the simplest method of following the course of change, apparently the polarimetric method is an unsuitable method, if the object be to arrive at a quantitative interpretation of the entire course of change; the chemical method, which permits of the measurement of the products of an interaction throughout the period of change, would seem to be the only one that can be used for such a purpose. Unfortunately the experimental errors incidental to chemical methods are usually so considerable that the minor departures to be detected are likely to escape observation, apart from the fact that the labour involved is usually very great.

*Rate at which Cane Sugar is Hydrolysed under Different Conditions of Concentration.*

Although the effect of varying the proportions of sugar and of acid has been studied more or less fully by previous workers, no systematic observations have been made on the extent to which variations over a wide range in the amount of water present affect the rate of change.

At the outset of the inquiry, therefore, three sets of experiments were carried out in each of which water was the variable, a different proportion of sugar being used in each series in order that any influence exercised by the concentration of the sugar might be discovered. In each series, a single molecular proportion of hydrogen chloride was present together with either one-quarter,

TABLE II.  
*Hydrolysis of Cane Sugar by One Molecular Proportion of Chlorhydric Acid.*

Water.	Sugar.		
	$\frac{1}{4}$ molecular proportion. K.	$\frac{1}{2}$ molecular proportion. K.	1 molecular proportion. K.
30	1282	1282	1277
		1276 1278	
40	808 806 806 804	815.5 818.5	800 799 796 797 799
		817	
50	583 578 579	585 580	579 582
			580.5
60	449 448	448.5 455.5	450 455
			452.5
80	303.5	303.5	307
			307.5
100	228 229	228.5 229	228 230
			229.5
200	100.5	100.5	101
			101

one-half or a single molecular proportion of sugar in a solution containing from 30 to 200 molecular proportions of water. As in all other cases considered, the action took place at 25°. The results are recorded in table II.

*Influence of the Concentration of the Sugar.*

The values of K given in the table are deduced from experiments made before the method of calculation explained in a previous section was developed. As the readings were taken some time after

mixing the solutions, it was impossible to deduce initial values by extrapolation. In order to obtain comparable data, values of  $K$  were determined at the stage of change when the action was approximately one-half or three-quarters complete; it was therefore possible to infer what amount of water was present and to deduce the value corresponding with a definite concentration. When subsequently the form of the curve expressing the relationship between the values of  $K$  and the concentration of the acid was ascertained, values were calculated by interpolation for solutions of the strength prepared; these are given in the table.\*

The experimental errors involved in the determination are probably greater in the case of solutions containing one-half and a single molecular proportion of sugar, as these were first examined before practice had been gained in utilising the various refinements referred to in the previous communication.

It is evident that changes in the concentration of the sugar have very little effect on the value of  $K$  at any of the dilutions considered. It is impossible to say from the numbers whether the effect be to increase or to decrease the value as the concentration of the sugar is increased from one-quarter to one molecule or whether there be no effect at all. The values obtained in the case of the solutions containing half a molecular proportion of sugar are apparently the highest but, as already pointed out, the errors may well have been greater in this series than in the others; in fact, this must be assumed to be the case, judging from later experience.

It is clear that when the solutions are dilute, the effect of considerable variations in the concentration of the sugar is extremely small. Later on, when the method had been fully developed and more skill had been gained in carrying on the observation, the effect of an alteration of the concentration of sugar was again considered—this time over a much wider range of concentration of sugar. In the solutions examined, the water and acid (nitric) were kept at a molecular concentration of 60 and 1 respectively, whilst that of the sugar was varied from 0·1 to 2·5. The results obtained are displayed in table III and also in Fig. 2. They upset the accepted belief that the rate of hydrolysis is proportional to the concentration of the sugar when sugar is the only variable.

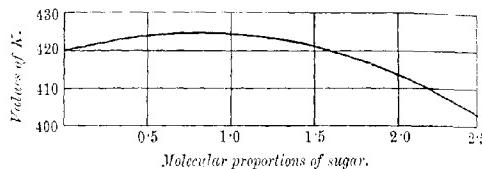
\* These values are to be regarded as approximate, as the method by which they are deduced involves the assumption that the rise in the values of  $K$  is conditioned only by the disappearance of water and the consequent concentration of the acid, any other possible cause of alteration in the values of  $K$  being left out of account. In the case of experiments with the smallest proportion of sugar ( $\frac{1}{2}$  molecular proportion), the errors involved must be very small, as in the more dilute solutions of this series no appreciable rise is manifest in the values of  $K$  throughout an experiment; even in those containing a small proportion of water the increase is not great.

TABLE III.

Sugar.	<i>K.</i>	Mean.
0·1	421	421
0·25	422	422
1·0	424	424
	424	
1·5	421	421
2·0	412	413
	413	
2·5	403	403

As the concentration of sugar is increased, the value of *K* at first rises slowly, reaching a maximum when the molecular concentration of sugar is approximately unity; it then decreases somewhat

FIG. 2.



rapidly as the concentration of sugar is further increased. This behaviour is probably conditioned by a variety of causes and cannot well be regarded otherwise than as proof that the change usually considered so simple is in reality of a very complex character.

The change in concentration of the sugar as the sugar disappears in any experiment must affect the successive values of *K* but the method by which *K* is arrived at, explained in a previous section, serves to eliminate this effect, as the value determined is that which characterises the solution at the commencement of change.

#### Degree of Hydration of the Acid System.

It is generally recognised that the rate at which sugar is hydrolysed by acids is roughly proportional to the concentration of the acid. Nevertheless, it is very difficult to discuss the exact way in which the activity of an acid varies with the concentration, as it is clearly impossible to vary the concentration of an acid in a known way. In an aqueous solution, the acid is combined with and in some way controls more or less of the water, so that if different amounts of acid be present the amount of uncombined water will vary according to the amount of acid present: the amount of water combined in the acid system being unknown, it is practically

impossible to arrange that a definite proportion of free water shall be present in a given solution of the acid.

The data used in discussing this question are derived from experiments with chlorhydric and nitric acids, in which only a

FIG. 3.

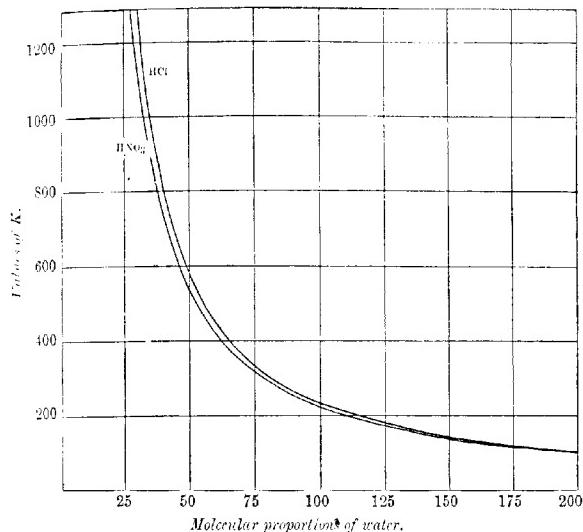


TABLE IV.

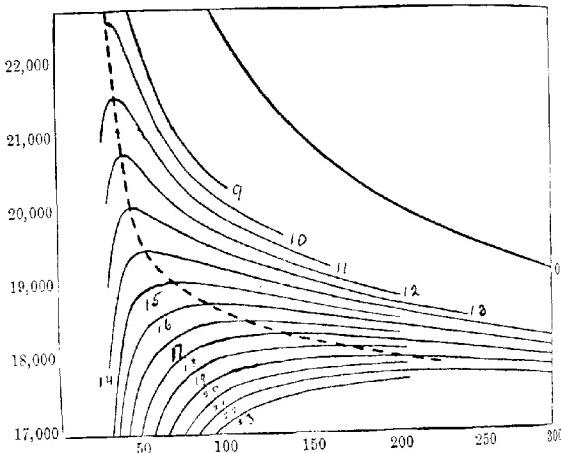
*Hydrolysis of Cane Sugar (1/4 Molecular Proportion) by One Molecular Proportion of Nitric Acid.*

Water.	$K'$ .	Mean.
30	1126	1126
40	741	740
50	549	540
60	422	422
80	292.2	292.4
100	223.1	222.9
200	100.1	100.1
	63.8	63.8

quarter-molecular proportion of sugar was used; the values are those given in tables II and IV. They are shown graphically in Fig. 3.

The rough proportionality between the values of  $K$  and the concentration of the acid which is obvious on considering the results recorded in tables II and IV is of such a character as to favour the assumption that the divergence from true proportionality may possibly be due to the disappearance of water and that if allowance were made for the combined water proportionality would become obvious. This consideration has led to a novel method of discussing the results being devised; the results obtained by the application of this method are not only highly interesting but appear to be of a rational character.

FIG. 4.



The method is best explained by reference to Fig. 4. Along the horizontal axis is given the total water present in molecular proportions (one molecular proportion of acid being always present), whilst along the vertical axis is given a set of values of the product of  $K$  into the number of molecules of water left free on the different assumptions that are possible as to the number of molecules controlled by the acid. The diagram is best understood by considering an individual curve—say that numbered 14. This curve, which is the outcome of the assumption that 14 molecules of water are associated with one of acid, was arrived at in the

following way. The successive values of  $K$  deduced from observations with solutions containing 30, 40, 50, 60, etc., molecular proportions of water were multiplied by 30-14, 40-14, 50-14, 60-14, etc., respectively; each product was then indicated on the ordinates through 30, 40, 50, 60, etc. The other curves were arrived at by assuming that the number of molecules expressed by the number on the curve was controlled by the acid.

What was sought for was the condition of hydration when  $K$  was proportional to the molecular concentration of the "acid system"—in other words, the *hydrated acid*.\*

As the "degree of hydration" probably increases as the solution is diluted, there can be only one concentration corresponding with a particular point on each curve at which the degree of hydration is that assumed. In the more concentrated regions on the left, the rise in the curve is an indication that the product of  $K$  into free water increases as the solution is diluted; whilst in the weaker solutions the fall of the curve is an indication of the decrease of this product. At the maximum, the product neither increases nor decreases; this may be regarded as the point sought for.

As a greater degree of hydration is assumed, the positions of the maxima on successive curves occur at points indicative of greater degrees of dilution—in other words, the acid system is more highly hydrated the greater the degree of dilution. The result is one which is to be anticipated on general grounds. A curve drawn through the several maxima expresses the change in the value of the product of  $K$  and free water (in other words, the ratio of  $K$  to the concentration of the hydrated acid) as the degree of hydration increases as the solution is diluted; moreover, it expresses the fact that not only does the system vary in composition and become more hydrated but also that it diminishes in activity as dilution proceeds.

Table V gives the values which we shall call the apparent hydration values of the acids for chlorhydric acid and for nitric acid as the total water is increased and also the corresponding molecular hydrolytic activities of the acids.

It should be pointed out that the water controlled by the sugar

\* The expression molecular concentration of the acid is here used to imply the molecular ratio of acid to *free* water. Thus in a solution prepared with 40 molecular proportions of water and one of the acid hydrolyst, assuming this to be associated with  $n$  molecules of water, the concentration is  $\frac{1}{40-n}$ . The ratio of  $K$  to this concentration is obviously  $K(40-n)$ . These are the values made use of in plotting the curves in Fig. 4. The "acid-system" must be supposed to include the hydrolyte with its attached water: in fact the whole of the water that is not *free*, either because it is attached or controlled; the assumption is made moreover—which is probably not a correct one—that the *free* water is ordinary water.

TABLE V.

*Apparent Molecular Hydration Values of Chlorhydric and Nitric Acids at different degrees of dilution and the corresponding molecular hydrolytic activities of the acid systems.*

Dilution (molecular proportions of water to one of acid).	Apparent molecular hydration.		Relative molecular hydrolytic activities.	
	HCl	HNO <sub>3</sub>	HCl	HNO <sub>3</sub>
30 .....	12.4	10	225	225
40 .....	13.6	12.3	211	205
50 .....	15.1	13.8	202	196
60 .....	16.8	14.6	193	192
80 .....	18.7	15.7	186	188
100 .....	19.8	16.6	182	186
200 .....	—	20.0	—	189

is not taken separately into account, the values arrived at being those for the total water controlled. As, however, the concentration of the sugar was very small in the experiments from which the values of  $K$  were derived and as sugar is probably not largely hydrated, the portion of the water not associated with the acid is probably very small. In order to eliminate this it would be necessary to work from values of  $K$  corresponding with infinitesimal concentrations of sugar.

The results of similar experiments carried out by E. Wheeler using cane sugar and hydrogen bromide and iodide and by W. H. Glover using raffinose and hydrogen chloride, hydrogen bromide and hydric nitrate have been discussed in a similar way and similar results have been arrived at—the degree of hydration of the acids always following the order of their activities. Moreover, the hydration values arrived at from W. H. Glover's experiments in which raffinose was used as the hydrolyte are practically the same as those arrived at by using cane sugar in the case of both the acids used—this is an important confirmation of the validity of the method. These results will be discussed in parts XIV and XVII.

Lastly, attention may be drawn to the remarkable similarity in the values given in table V as the relative molecular hydrolytic activities of the two acid systems in solutions containing equal total amounts of water. To determine the precise relationship of the two acids, it will be necessary to amplify the data so that the values are placed beyond question.

#### *Effect of Salts on the Rate of Hydrolysis by Acids.*

Apparent "hydration" values have been deduced for salts by Caldwell, Whymper and others, who found by trial how much

water must be added to a system containing water, sugar, acid and salt to reduce the hydrolytic activity of the system to that of a similar system from which salt was absent. A set of values for different salts was arrived at in this way but only one dilution was studied. The method has been applied to a larger number of salts in solutions varying considerably in concentration.

The rate of hydrolysis was determined, as in the case of the acid alone, in solutions containing one molecular proportion of acid, one-quarter of sugar, one of salt and 60, 80, 100 respectively of water. In the case of chlorhydric acid, the chlorides of lithium, sodium, rubidium and caesium were examined; in the case of hydric nitrate, the nitrates of lithium, sodium, potassium, rubidium, caesium, silver and calcium. The results are recorded in tables VI and VII. As the value of  $K$  is always increased by the presence

TABLE VI.

*Influence of Chlorides on the Rate of Hydrolysis of Cane Sugar by Chlorhydric Acid. Sugar  $\frac{1}{4}$ , acid 1, salt 1, water 60, 80 and 100 molecular proportions.*

Water.	$K$				
	HCl alone	LiCl	NaCl	RbCl	CsCl
50 .....	580	—	833	—	—
60 .....	448·5	628	610	578	562
80 .....	303·5	395	388	370	364
100 ...	228·5	284	280	270	267

TABLE VII.

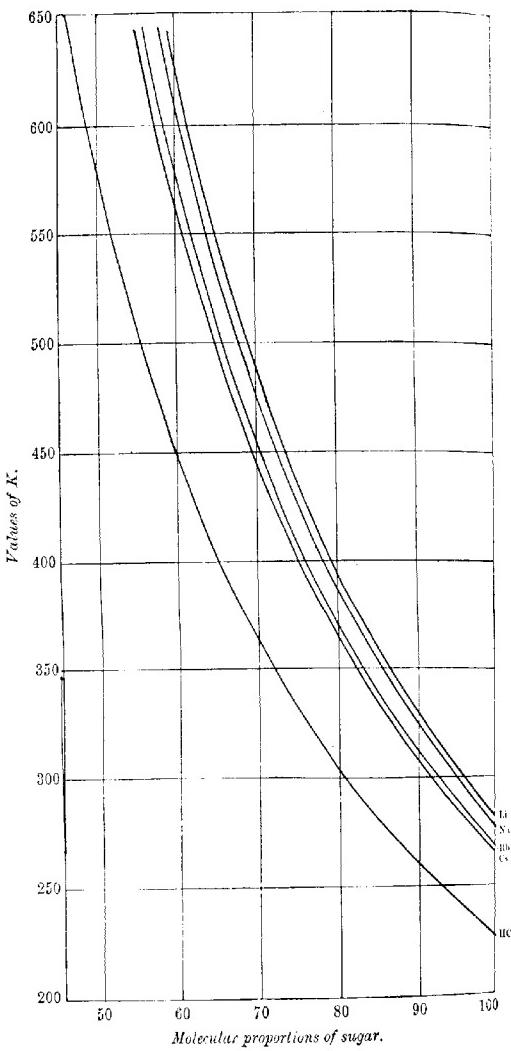
*Influence of Nitrates on the Rate of Hydrolysis of Cane Sugar by Nitric Acid. Sugar  $\frac{1}{4}$ , acid 1, salt 1, water 60, 80 and 100 molecular proportions.*

Water.	$K$							
	HNO <sub>3</sub> alone	LiNO <sub>3</sub>	NaNO <sub>3</sub>	KNO <sub>3</sub>	RbNO <sub>3</sub>	CsNO <sub>3</sub>	AgNO <sub>3</sub>	Ca(NO <sub>3</sub> ) <sub>2</sub>
60... 422	565	534	504	495	486	476	—	—
80... 292·4	368	353	339	335	331	321	324	—
100... 222·9	269	261	252	251	247	—	—	303

of salts, when the results are plotted graphically the curves for the salts lies always to the right of the corresponding acid curve (Figs. 5 and 6). The apparent hydration values for any salt for any dilution within the range of the experiments can be read off directly from such curves as the horizontal distance between the curve for the particular salt and that for the corresponding acid.

Previously the apparent degree of hydration of the salt has been expressed as the molecular proportion of water that must be added when the salt is present to reduce the value of  $K$  to that found in the absence of the salt. It is obviously a better method

FIG. 5.



metal in the salt increases. This may be due to the fact that the effect of the salt on the rate of hydrolysis is due to a variety of causes acting in opposite directions, among others to a concentrating effect -conditioned by a withdrawal of water by the salt—which increases the rate of hydrolysis and to a mechanical effect tending to diminish it: this mechanical effect probably increases as the mass of the molecule increases; moreover salts are probably present in solution to a greater or less extent in the form of "associated" molecules. For these various reasons it is impossible at present to institute any effective comparison between salts in explanation of the observed differences in the degree of hydration.

Attention may be drawn to the similarity between the curves for the hydration values of the salts and those of the corresponding acids; this may be regarded as confirmation of the validity of the method of arriving at the degree of hydration of acids advocated in this communication.

*Summary.*—Owing to the improved appliances available, the hydrolysis of cane sugar by acids has been studied more thoroughly and with closer approach to accuracy than has before been possible. It has been found not only that there are unexpected sources of error in the method adopted by previous workers but also that the accepted views which have hitherto guided inquirers in this field need modification in essential particulars.

The chief points in the present communication are the following:

(1) The end-point usually observed when the sugar is judged to be entirely inverted is not the true end-point but an erroneous value, as the rotatory power at the end of the hydrolysis does not remain constant but gradually becomes less and less negative, on account of a secondary change affecting the products of hydrolysis. Although probably it is unimportant in the case of dilute solutions, this change cannot be neglected in concentrated solutions; in the case of such solutions, the corrected end-point must be deduced from observations of the rate of change after the rise sets in.

(2) The values of  $K$  obtained by applying the unimolecular equation  $dx/dt = K(a-x)$ , except in the case of very dilute solutions, are not constant but rise as hydrolysis proceeds; in other words, the action does not follow the unimolecular law. Moreover, if the action be treated as a case of bimolecular change in which the rate of change is proportional to the mass of water present as well as to the amount of sugar, no better result is arrived at, the rise in the values of  $K$  thus deduced being greater than when the unimolecular expression is applied.

(3) The usual method of applying the mass action equation is

not the best. Besides a possible general error due to an incorrect initial reading, it gives a spurious constancy to the values of  $K$ , making it difficult to detect actual departures from the unimolecular law. A better way of applying the equation is in the form:

$$K \log e = \frac{1}{t_2 - t_1} \log_{10} \frac{a - x_1}{a - x_2},$$

where  $a - x_1$  and  $a - x_2$  are the sugar concentrations at times  $t_1$  and  $t_2$  respectively—successive equal intervals of time being taken as small as the accuracy of the observations allows or the rapidity of the change demands.

(4) The observations are most satisfactorily dealt with by deducing values of  $K$  by the unimolecular equation for successive small intervals during each of which sugar is the only significant variable. If the successive values of  $K$  rise as hydrolysis proceeds, the value at the commencement of the change when the solution is of known composition and free from products of change should be found by extrapolation. Values of  $K$  must be obtained as near the beginning of the interaction as possible; for this purpose, it is essential that the solution should be mixed at the temperature at which the experiment is to be made and readings of the rotation taken as soon as constant temperature can be obtained.

(5) It has been found that the fundamental assumption that the rate of hydrolysis is proportional to the concentration of the sugar is only an approximation. If sugar be made the only variable in a series of experiments, the values of  $K$  at first rise slowly and after reaching a maximum fall rapidly as the concentration of the sugar is increased. In studying the effect of acids and salts or other substances on the rate of hydrolysis, it is essential to use as low a concentration of sugar as possible, as the effect of the change in the sugar is practically negligible in weak solutions.

(6) From the rate of change of  $K$  when the concentration of the acid is varied, a method has been developed by means of which the apparent degree of hydration of the acid at different dilutions may be determined. This increases with dilution towards a maximum and at the same time the molecular hydrolytic activity of the acid decreases towards a minimum.

(7) From the influence of a number of chlorides and nitrates in increasing the rate of hydrolysis brought about by chlorhydric and nitric acids respectively, apparent hydration values of the salts have been determined at different dilutions. The values so determined are probably low on account of mechanical inhibiting effects and other influences exercised by the salts—they are less in the case of chlorides and nitrates of the alkali metals than in those of

the corresponding acids and decrease as the atomic weight of the metal increases.

(8) This investigation emphasises the need of taking into account the complexity of the changes involved in the hydrolysis of cane sugar under the influence of acids and shows the futility of attempting to express the rate of such an interaction by any simple mathematical equation. Although the rate of hydrolysis is nearly proportional to the concentration of the sugar and to the concentration of the *hydrated acid*, a true mathematical expression of the rate under various conditions of concentration of the interacting substances would involve, besides factors for the concentration of the sugar and the hydrated acid, numerous other factors allowing for the fact that the rate of hydrolysis is not strictly proportional to the concentration of the sugar and that the degree of hydration of the acid and also its molecular hydrolytic activity alter on dilution; in addition it would be necessary to take into account the effect of the primary products of change as well as their further change and also changes in the state of aggregation and changes in the optical rotatory power of the various components of the solution; it is obviously undesirable to attempt such an expression. Many of these factors influencing the rate of change are no doubt extremely small but may not be negligible under all conditions.

It is hoped that this investigation will have thrown light on the chief laws regulating the rate of hydrolytic change and that it may serve to indicate clearly what are the conditions under which it is legitimate to use the hydrolytic process as a means of studying the problems afforded by solutions.

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XLVI.—*Studies of the Processes Operative in Solutions*  
Part XIV. *The Determination of Apparent  
Hydration Values by means of Raffinose.*

By WALTER HAMIS GLOVER, Ph.D., Salters' Company's Research Fellow, City and Guilds of London Institute, Central Technical College.

THE present communication contains the results of a number of observations on the hydrolysis of raffinose, a triose having the formula  $C_{18}H_{32}O_{16} \cdot 5H_2O$ , by nitric acid, chlorhydric acid and bromhydric acid and of the influence of certain salts of these

acids, in particular the salts of the alkali metals, on the velocity with which the sugar is converted into melibiose and fructose. The investigation was carried out primarily with the object of ascertaining whether and to what extent the substitution for cane sugar of raffinose—a compound which is similar to it in chemical properties—is attended by a difference in the apparent "hydration values" of the salts. Brief reference has been made by Armstrong and Crothers (Part VIII, p. 110) to the result of an experiment which appeared to indicate that the concentrating effect produced by the addition of one molecular proportion of sodium nitrate to an aqueous solution of one molecular proportion of nitric acid and one-quarter molecular proportion of raffinose is not so great as that induced when the hydrolyte is cane sugar; in other words, the "hydration value" of sodium nitrate determined by hydrolysing raffinose by nitric acid in the presence of sodium nitrate was  $8H_2O$  instead of  $11H_2O$ , the value obtained by Whympner by means of cane sugar (Part III, p. 579). A difference of this nature was not altogether surprising when viewed in the light of the results recorded by Armstrong and Watson (Part IV). It is shown in this paper that the "hydration values" determined with the aid of methyl acetate are vastly different to those deduced from the hydrolysis of sucrose. It may be stated at once, however, that the "hydration values" derived from the experiments with raffinose are almost identical with those arrived at when cane sugar is used as the hydrolyte in the case of chlorides, although in the case of the nitrates the values are uniformly slightly smaller.

Before proceeding further with the discussion on the effect of salts on the rate of hydrolysis of raffinose by acids, it will be advisable to contrast the behaviour of cane sugar and raffinose towards acids from the point of view of the readiness with which the fructose section of the sugar molecule is split off.

The course of the interaction between one molecular proportion of acid and a one-quarter molecular proportion of raffinose in aqueous solution has been investigated, the proportion of water ranging from 40 to 100 molecules; the results are recorded in table I. It will be seen that the velocity, as represented by  $K(1/t \log a - x)$ , is not inversely proportional to the quantity of water present; instead, the product  $K \times$  number of molecules of water becomes smaller as the dilution of the interacting substances becomes greater. Neither does the "volume molecular hydrolytic activity"\*\* of the acid remain constant. In order to arrive at this

\* "Volume molecular hydrolytic activity" =  $K \times$  vol. in litres containing 1 molecular proportion of acid; it represents the rate at which the sugar would be hydrolysed provided 1 litre of the solution contained 1 molecular proportion of acid having the same activity as that in the solution under investigation.

quantity, the densities of the solutions at 25° containing 1 molecular proportion of nitric acid and 0·25 of a molecular proportion of raffinose (anhydrous) in 50 and in 100 molecular proportions of water were determined and found to be 1·0802 and 1·0425 respectively; from these values the volumes of the solutions were calculated to be 1008·2 c.c. and 1907·9 c.c. respectively; assuming the hydrolytic activity of the acid to be proportional to the concentration of the acid per unit volume, we have

$$A_1 = 458·7(485 \times 1·0082)$$

and  $K_1 = 354·8(186 \times 1·9079)$  as the "volume molecular hydrolytic activities" of the nitric acid at the two dilutions. The fact that the addition of 50 molecular proportions of water (900 grams) to the stronger solution increases the total volume by approximately its own volume is not without interest.

The apparent hydration values have been deduced by means of the method developed by F. P. Worley, in Part XII of these studies. On contrasting the values with those obtained by Worley using cane sugar as hydrolyte, it is obvious that the two sugars afford practically identical values.

It is extremely difficult to interpret such results, as although a fairly simple relationship exists between the rate of change of the sugar and the amount of "free" water (total water -  $x$ ), there can be little doubt that dilution is accompanied by a great many changes in the complexity and nature of the components of the system under examination. The nature of many of these changes has been discussed in Part VI of these studies; the following may also be cited as exemplifying the great variety of changes which possibly accompany any alteration in the molecular proportions of the components. The hydrolysis of a sugar by an acid undoubtedly takes place in an unstable system containing acid, sugar and water; one effect of an increase in the proportion of water would be to dissociate or retard the formation of this system and consequently to diminish the "molecular hydrolytic activity" of the acid.

Before leaving the subject of the hydrolysis of raffinose by acids, attention must be drawn to a remarkable relationship which exists between the rates at which cane sugar and raffinose are hydrolysed. In the case of the three acids used in this investigation, it is found that cane sugar is always hydrolysed by the same solution of an acid at a rate 1·195 times (mean value) greater than raffinose; this is shown by the following table:

Molecules of water.	Values of $\frac{K(\text{cane sugar})}{K(\text{raffinose})}$ .		
	HNO <sub>3</sub>	HCl.	HBr.
40	1.193	1.199	1.195
50	1.185	1.203	1.184
60	1.196	1.198	1.186
70	1.192	1.186	1.200
80	1.196	1.193	1.201
90	1.200	1.203	1.203
100	1.194	1.194	1.194
Mean.....	1.194	1.196	1.195

The fact that the cane sugar section of the molecule of raffinose is less readily hydrolysed than is cane sugar itself has been explained partly by the assumption that raffinose is the weaker because it is a less hydrolyzed hydrolyte (compare Armstrong and Crothers, *loc. cit.*). Some experiments have been made which seem to indicate that the difference may be due largely to the degree in which combination takes place between the sugar and the acid, as indicated by the influence salts exercise on the specific optical rotatory power of sucrose and of raffinose. In each case, the proportions used were 0.5 gram-molecular proportion of anhydrous sugar + 1 gram-molecular proportion of anhydrous salt + 50 gram-molecular proportions of water, the values obtained being the following:

Sugar.	Salt.	$[\alpha]_{D}^{25}$		Reduction in $[\alpha]_{D}^{25}$ of sugar in percentages.
		Experimental values.	Mean.	
Cane Sugar.	—	78.06	78.06	—
	Potassium chloride ...	77.10	77.10	1.21
	" bromide ...	76.48	76.48	2.02
	" iodide.....	75.46	75.46	3.33
Raffinose.	...	145.46	145.55	—
	—	145.65		
	Potassium chloride ...	145.49	145.50	0.03
	" " ...	145.51		
	" bromide ...	145.23	145.235	0.22
	" " ...	145.24		
	" iodide... ..	144.56	144.62	0.64

Assuming the change of specific optical rotatory power to be due primarily to combination of sugar and salt, as dilution has practically no effect on the specific rotatory power of either cane sugar or raffinose, it is evident that under comparable conditions raffinose does not combine to so great an extent with salts as does cane sugar; it is to be inferred therefore that acids likewise do not combine so readily with the triose as with the biose and since hydrolysis of the sugar is undoubtedly preceded by the formation of a compound of acid, sugar and water, it naturally follows that raffinose would not be hydrolysed so readily as cane sugar.

Passing now to a consideration of the results obtained in the investigation of the influence of various salts on the rate of hydrolysis of raffinose by acids (tables I, II, III), we find the concentrating effect to be almost the same as that when cane sugar is the hydrolyte. This is well illustrated by the following table, in which are given the number of molecules of water which must be added to neutralise the accelerating or concentrating effect (apparent hydration values) of the salts in the case of the two sugars.

Salt.	Total number of mols. of water present per mol. of acid and salt.	Number of mols. of water to be added to the system.	
		Cane Sugar.	Raffinose.
Silver nitrate .....	50·0	—	3·3
	55·5	4·7 <sup>2</sup>	3·7
	60·0	5·0 <sup>2</sup>	4·0
Potassium nitrate.....	50·0	7·1 <sup>1</sup>	6·7
	55·5	—	7·2
	60·0	8·2 <sup>1</sup>	7·5
Sodium nitrate.....	50·0	9·5 <sup>1</sup>	8·8
	55·5	—	9·3
	60·0	10·6 <sup>1</sup>	9·6
Lithium nitrate .....	40·0	—	10·0
	50·0	11·8 <sup>1</sup>	11·4
	60·0	13·0 <sup>1</sup>	12·0
Ammonium chloride..	50·0	10·2 <sup>4</sup>	10·2
	55·5	10·9 <sup>4</sup>	10·8
	60·0	—	11·0
Potassium chloride ...	50·0	10·8 <sup>4</sup>	10·4
	55·5	11·1 <sup>4</sup>	11·0
	60·0	—	11·2
Sodium chloride .....	40·0	10·8 <sup>1</sup>	10·8
	50·0	12·0 <sup>1</sup>	12·2
	55·5	—	13·0
Calcium chloride .....	40·0	22·0 <sup>1</sup>	22·2
	50·0	23·2 <sup>1</sup>	24·2
	55·5	—	25·0
Potassium bromide ...	40·0	10·7 <sup>3</sup>	10·8
	50·0	12·0 <sup>3</sup>	11·8

<sup>1</sup> Deduced from F. P. Worley's values.

<sup>2</sup> Whynper.

<sup>3</sup> Wheeler.

<sup>4</sup> Deduced from Callwell's results.

The closeness of the values for the bromide and the chlorides obtained by using either cane sugar or raffinose as hydrolyte is truly remarkable; only in the case of the nitrates is a constant difference noticeable, the values derived from the use of raffinose being without exception slightly smaller than those obtained with cane sugar; it is also interesting to note that the hydration value of potassium bromide is higher than that of potassium chloride. All these observations are in accord with the explanation of the manner in which salts accelerate the rate of hydrolysis advanced in Part VIII of these studies. It is possible that part of the effect produced by

the addition of a salt to a solution of sugar and acid is due to the displacement, by the salt, of acid combined presumably with the hydroxylc and anhydride oxygen atoms of the sugar but this is not likely to be a very large effect. Neither is it probable that the retardation produced by the mechanical interference of the salt molecule is very great, although the effect produced by a series of salts, for example, the chlorides or nitrates of the univalent metals, becomes smaller as the weight or size of the molecule becomes greater.

#### EXPERIMENTAL.

The solutions were prepared in the flasks figured in Fig. 1, Part XII. No difficulty was experienced in obtaining the final readings; although the optical rotatory power of the solution does not remain constant at the end of the period of change under investigation, the alterations observed are too small to affect the constant  $K$ ; the optical rotatory power increases slightly at first after the chief action is completed, owing to changes of the fructose; it then decreases very slowly, possibly owing to the gradual hydrolysis of the melibiose.

*Materials Used.*--The sodium chloride was purified by precipitation from brine by hydrogen chloride, subsequently recrystallised from water and finally precipitated from an aqueous solution by alcohol; the ammonium chloride, potassium chloride, potassium nitrate, sodium nitrate and potassium bromide were crystallised repeatedly from water. The lithium nitrate and silver nitrate were commercially pure samples; when tested, they were found to be neutral. The requisite quantity of calcium chloride for each experiment was obtained by neutralising the calculated weight of standard hydrogen chloride solution with an excess of pure Iceland spar.

All the experiments referred to were performed at  $25.01^\circ \pm 0.005^\circ$ . The results obtained in two complete experiments with each acid entirely representative of the series are recorded in table IV.

TABLE I.  
*Hydrolysis of Raffinose by Acids.*  
0.25 Molecule of Raffinose (anhydrous) + 1 Molecule of Acid +  
a Molecules of Water.

Acid.	Molecules of water.	Values of $K$		Mean values of $K$
		Expt. I	Expt. II	
Nitric .....	40	620	624	622
	50	454.5	455	455
	60	357	354	355.5
	80	245	245	245
	100	185.5	185.6	185.5

TABLE I. (*continued*).

Acid.	Molecules of water.	Values of $K$		Mean values of $K$
		Expt. I	Expt. II	
Chlorhydric .....	40	672	672.5	672
	50	482	482.6	482
	50	375	373	374
	80	255.7	253.3	254.5
	100	192.4	190.6	191.5
Bromhydric .....	40	786	786.8	786
	50	555.2	556	556
	60	420	420	420
	80	277.8	278.2	278
	100	206.3	206	206

TABLE II.

*Hydrolysis of Raffinose by Chlorhydric Acid in the Presence of Certain Chlorides.*

0.25 Molecule of Raffinose + 1 Molecule of Hydrogen Chloride + 1 Molecule of Salt +  $\alpha$  Molecules of Water.

Salt.	Mean values of $K$			
	50 molecules of water.	60 molecules of water.	70 molecules of water.	80 molecules of water.
Ammonium chloride.....	656	484	381	—
Potassium .....	660	486	383	—
Sodium .....	680	511	402	433.5 (62H <sub>2</sub> O)
Calcium .....	1035	723	539	421

TABLE III.

*Hydrolysis of Raffinose by Nitric Acid in the Presence of Nitrates.*

0.25 Molecule of Raffinose (anhydrous) + 1 Molecule of Nitric Acid + 1 Molecule of Salt +  $\alpha$  Molecules of Water.

Salt.	Mean values of $K$		
	50 molecules of water.	60 molecules of water.	70 molecules of water.
Silver nitrate .....	499	389	314
Potassium nitrate.....	546	421	338
Sodium .....	580	412	354
Lithium .....	623	473	372

*Hydrolysis of Raffinose (0.25 Molecule) by Bromhydric Acid (1 Molecule) in the Presence of Potassium Bromide (1 Molecule).*

Molecules of water .....	50	60	70
Mean values of $K$ .....	808	587	451

TABLE IV.  
0-25 Gram-molecule of Raffinose (anhydrous) + 50 Gram-molecules of Water.

XLVII.—*Studies of the Processes Operative in Solutions.*  
*Part XV. The Changes Effected by the Reciprocal Interference of Sugars (and Glucosides) and Salts in Aqueous Solutions.*

By WALTER HAMIS GLOVER.

BRIEF reference is made by Armstrong and Crothers in Part VIII of these studies to the striking diminution of the conductivity of sodium chloride effected by the addition of raffinose. It is shown that the conductivity in a solution of a gram-molecular proportion of the electrolyte in 1000 grams of water is lowered to the extent of 21 per cent. by one-third of a gram-molecular proportion of the carbohydrate, whilst a reduction of 27·4 per cent. and 44·6 per cent. is produced by the addition of a gram-molecular proportion of glucose and cane sugar respectively. In other words, judging from these figures only, the conductivity of salts in solution is reduced by these sugars practically in proportion to the number of oxygen atoms which they contain.

The object of the investigation described in the present communication was to ascertain whether other salts are similarly affected, not only by the three carbohydrates just mentioned but also by the two reducing disoses, lactose and melibiose and by the two simple, non-reducing ethers of glucose,  $\alpha$ -methylglucoside and  $\beta$ -methylglucoside. At the same time, it was considered advisable to measure the effect on the specific rotatory powers of the several carbohydrates induced by the presence of the electrolyte, particularly with the object of testing a conclusion arrived at in an earlier investigation, namely, that the specific rotatory power of a carbohydrate which is hydrolysed by acids with relative ease is influenced to a greater degree by the presence of a salt than is the specific rotatory power of a carbohydrate less open to hydrolytic attack by acids.

*Preparation of Solutions.*—The salts and other substances used, with the exception of the glucose and cane sugar, were purified with care. The glucose used was the purest material obtainable from Kahlbaum; the cane sugar that sold as "coffee sugar" or "centrifugals."

The solutes were weighed out in a conical Jena-glass flask, due allowance being made for the air displaced. Approximately the right quantity of "conductivity" water was then run in and the solid dissolved by gently warming the flask. After cooling to the temperature of the room, the weight of water was adjusted to the required amount on the balance. In calculating the quantity of

solvent to be added, due allowance was always made for the water already in combination with the non-electrolyte as "water of crystallisation."

*Determination of Rotatory Power.*—Except for certain improvements, the apparatus and methods used are described in previous communications; the measurements were made in water-jacketed tubes 400 mm. long. In cases in which the sugar undergoes mutarotation, the solutions were kept during twenty-four to forty-eight hours before the measurements were made. The specific rotatory powers recorded in this paper without exception refer to the anhydrous sugar.

*Determination of Density.*—The densities of the solutions at 25° were measured with the aid of the modified form of Sprengel tube described by Caldwell and Whymper (Part X).

*Measurement of Conductivity.*—The readings were taken with a Kohlrausch wheel-bridge, inductorium and telephone. The resistance of the electrolytic cell, the form used being that described by Caldwell and Whymper (*loc. cit.*), was as nearly as possible balanced by coils of known resistance wound non-self-inductively, so that the readings could always be taken at points close to the middle of the bridge-wire. Corrections were made for inequalities of the bridge-wire and resistance of the leads.

*Effect of Salts on the Optical Rotatory Power of Glucosides and Sugars.*—A vast amount of work has been done on the effect of salts on the optical rotatory power of glucose, lactose and cane sugar but much of it is valueless, as the molecular proportions of sugar and water were not kept constant; almost without exception the sugar and salt have been dissolved in water and the mixture made up to a known volume.

The specific rotatory powers of the substances used were found to be as follows:

One gram-molecule of substance in 50 gram-molecules of water.

	D <sub>25</sub> 25	[α] <sub>D<sub>25</sub></sub> H <sub>2</sub> O
Glucose.....	1·0655	+ 63·17°
α-Methylglucoside .....	1·05915	+ 186·50
β-Methylglucoside .....	1·05845	- 39·81
Cane sugar .....	1·11985	+ 78·08

Half gram-molecule of substance in 50 gram-molecules of water.

	D <sub>25</sub> 25	[α] <sub>D<sub>25</sub></sub> H <sub>2</sub> O
Glucose.....	1·03542	+ 62·73°
α-Methylglucoside .....	1·03162	+ 186·37
β-Methylglucoside .....	1·03127	- 39·58
Lactose .....	1·06634	+ 64·54
Maltose .....	1·06705	+ 168·93
Cane sugar .....	1·06490	+ 78·06
Raffinose .....	1·09331	+ 145·55

The changes of optical rotatory power produced by the addition of the various salts are recorded in tables I and II.

*Alteration in the Rotatory Power of Certain Sugars and Glucosides conditioned by Electrolytes.*

TABLE I.

One gram-molecule of electrolyte and 0·5 gram-molecule of sugar or glucoside in 50 gram-molecules of water.

Electrolyte,	Sugar or glucoside,	Density of solutions $D_{25}^{25}$	Values of $[\alpha]_{D}^{25}$	Alteration of $[\alpha]_{D}^{25}$	
				In degrees.	In per cent.
Potassium chloride	Glucose .....	1·07958	+ 61·40 <sup>2</sup>	- 1·33	- 2·12
	$\alpha$ -Methylglucoside ...	1·07584	+ 185·95	- 0·42	- 0·22
	$\beta$ -Methylglucoside ...	1·07553	- 40·30	- 0·72	- 1·82
	Lactose.....	1·10728	+ 64·65	+ 0·11	+ 0·17
	Melibiose.....	1·10792	+ 169·21	+ 0·31	+ 0·18
	Cane sugar .....	1·10583	+ 77·10	- 0·96	- 1·23
	Raffinose .....	1·13128	+ 145·51	- 0·04	- 0·03
Sodium chloride	Glucose .....	1·07454	+ 62·42	- 0·31	- 0·49
	$\alpha$ -Methylglucoside ...	1·07066	+ 185·85	- 0·52	- 0·28
	$\beta$ -Methylglucoside ...	1·07034	- 49·38	- 0·80	- 2·02
	Lactose.....	1·10247	+ 65·45	+ 0·91	+ 1·41
	Melibiose.....	1·10312	+ 169·38	+ 0·45	+ 0·27
	Cane sugar .....	1·10134	+ 76·80	- 1·26	- 1·61
	Raffinose .....	1·12707	+ 145·53	- 0·02	- 0·02
Potassium bromide	Cane sugar .....	1·14179	+ 76·48	- 1·53	- 2·02
	Raffinose .....	1·16572	+ 145·24	- 0·31	- 0·21
Potassium iodide	Cane sugar .....	1·17360	+ 75·46	- 2·60	- 3·33
	Raffinose .....	1·19563	+ 144·62	- 0·33	- 0·64

TABLE II.

One gram-molecule of sugar or glucoside and 1 gram-molecule of electrolyte dissolved in 50 gram-molecules of water.

Electrolyte,	Sugar or glucoside,	Density of solutions	Values of $[\alpha]_{D}^{25}$	Alteration Alteration, in degrees. per cent.	
				in degrees.	per cent.
Sodium chloride	Glucose .....	1·10231	+ 62·82 <sup>2</sup>	- 0·35	- 0·56
	$\alpha$ -Methylglucoside ...	1·09465	+ 185·98	- 0·52	- 0·27
	$\beta$ -Methylglucoside ...	1·09413	- 40·55	- 0·74	- 1·86
	Cane sugar .....	1·14812	+ 76·94	- 1·14	- 1·46
	Glucose .....	1·11574	+ 62·78	- 0·39	- 0·62
	$\alpha$ -Methylglucoside ...	1·10713	+ 186·39	- 0·11	- 0·06
	Cane sugar .....	1·15988	+ 77·52	- 0·56	- 0·72

The following are the most noteworthy conclusions to be drawn from an examination of the figures contained in these tables:  
(1) The effect produced by the addition of a salt to a non-reducing sugar or a simple glucoside is to render it less dextrorotatory; that is, in the case of the dextrorotatory compounds the apparent specific rotatory power is diminished, whilst in the case of the levorotatory

$\beta$ -methylglucoside the apparent specific rotatory power is increased. Assuming the change to be produced by combination of the non-electrolyte with the salt (as the specific rotatory powers of the substances at present under discussion do not alter appreciably on dilution, the changes cannot be ascribed to a withdrawal of water from the system by the salt) and that the combination involves the

formation of compounds of the type  $\begin{array}{c} \text{C}-\text{C} \\ | \\ \text{C}-\text{C} \end{array} >\text{O:XR}$ , the alteration

in the optical activity produced by the ethenoid link is in these cases levo-rotatory. Further, in the case of closely related substances which exist in solution in only one form, it is noticeable that the compound which is most stable towards hydrolytic agents is least affected by the salt. Thus, the change of optical rotatory power of  $\beta$ -methylglucoside under comparable conditions is much greater than that of the  $\alpha$ -isomeride; the  $\beta$ -compound is hydrolysed by acids 1.8 times as rapidly as the  $\alpha$ -isomeride. Similarly, cane sugar, which is hydrolysed about 1.2 times as rapidly by acids as raffinose, is more affected than the latter carbohydrate, which is a derivative of cane sugar.

(2) The changes of optical rotatory power exhibited by the reducing sugars are extremely complex. The dextrorotatory disaccharides, lactose and melibiose, unlike all the other substances studied, become apparently more dextrorotatory in the presence of salts. Further, although in the case of the non-reducing sugars the effect produced by a molecular proportion of sodium chloride is always slightly greater than that induced by potassium chloride or sodium nitrate, the effect in the case of the reducing sugars varies considerably according to the nature of the components; thus, glucose is apparently less dextrorotatory in the presence of sodium nitrate or potassium chloride than of sodium chloride; again, potassium chloride appears to change the closely related sugars, lactose and melibiose, to practically the same extent, whilst sodium chloride has a far greater effect on lactose than on melibiose.

It is evident, then, that the effect on the optical rotatory power of a sugar or glucoside produced by the presence of a salt cannot be ascribed to any one simple cause, although the principal factor at work is undoubtedly union of the several components of the solution; the marked divergences in the case of the reducing sugars which exist in solution in two stereoisomeric forms are principally due to a change in the state of equilibrium of the isodynamic forms.

*Effect of Glucosides and Sugars on the Electrical Conductivity of Salts.*—The molecular conductivities of the salts used, in solutions containing a gram-molecular proportion of salt in 50 gram-molecular proportions of water, were found to be as follows: potassium

chloride, 111.44; sodium chloride, 84.35; sodium nitrate, 75.03. The molecular conductivities in the presence of the various glucosides and sugars are given in tables III and IV.

*The Effect of certain Sugars and Glucosides on the Molecular Conductivities of Electrolytes.*

TABLE III.

One gram-molecule of electrolyte and 0.5 gram-molecule of sugar or glucoside in 50 gram-molecules of water.

Electrolyte.	Sugar.	Molecular conductivity of electrolyte.	Reduction of molecular conductivity, per cent.
Potassium chloride	Glucose.....	92.86	16.7
	$\alpha$ -Methylglucoside .....	90.53	18.8
	$\beta$ -Methylglucoside .....	90.77	18.5
	Lactose .....	78.38	29.6
	Melibiose .....	77.31	30.6
	Cane sugar .....	80.34	27.9
Sodium chloride	Raffinose .....	67.38	39.5
	Glucose .....	70.88	16.0
	$\alpha$ -Methylglucoside .....	68.94	18.3
	$\beta$ -Methylglucoside .....	69.21	17.9
	Lactose .....	59.88	29.0
	Melibiose .....	59.30	29.7
Cane sugar .....	Cane sugar .....	60.82	27.9
	Raffinose .....	51.33	39.1

TABLE IV.

One gram-molecule of sugar or glucoside and 1 gram-molecule of electrolyte in 50 gram-molecules of water.

Electrolyte.	Sugar or Glucoside.	Molecular conductivity of electrolyte.	Reduction of molecular conductivity, per cent.
Sodium chloride	Glucose.....	59.44	29.5
	$\alpha$ -Methylglucoside .....	56.50	33.0
	$\beta$ -Methylglucoside .....	56.80	32.6
	Cane sugar .....	44.16	47.6
Sodium nitrate	Glucose.....	53.28	29.0
	$\alpha$ -Methylglucoside .....	50.94	32.1
Cane sugar .....	Cane sugar .....	39.68	47.1

The probable manner in which sugars influence the conductivity of salts has been discussed in previous communications; the results of the experiments to be recorded in Part XVIII of these studies show, however, that although the diminution of conductivity is undoubtedly intimately connected with the number of hydroxyl groups in the molecule of the added non-electrolyte, nevertheless other factors play an important part in bringing about the diminution of conductivity.

An example of this is supplied by the isomeric methylglucosides,

which do not reduce the conductivity to the same extent; the effect produced by the  $\beta$ -isomeride is uniformly smaller than that produced by the  $\alpha$ -compound, although from the change of optical rotatory power it may be inferred that the  $\beta$ -compound unites to a greater extent with the salt than does the  $\alpha$ -isomeride.

Although they contain the same number of oxygen atoms in the molecule, the methylglucosides exert a greater influence than glucose itself; this is rather remarkable, seeing that the reducing sugar probably combines more readily with salts than its ethers; possibly in this case the mechanical effect of the non-electrolyte, due to the size of the molecule, comes into play. As indicating a relationship between the magnitude of the molecule and the effect produced, it is interesting to note that the displacement of a hydrogen atom in glucose or cane sugar by the  $C_6H_{11}O_5$  group results in an increase in the reduction of conductivity of about 11.5 per cent. (in solutions containing a gram-molecular proportion of potassium or sodium chloride and 0.5 gram-molecular proportion of sugar in 50 gram-molecular proportions of water).

The reduction of conductivity produced by lactose or melibiose is greater than that effected by cane sugar; possibly the reducing sugars combine with a greater proportion of the salt or as they both crystallise with water, melibiose with two molecules and lactose with one molecule, their greater activity may be due to the withdrawal of a larger proportion of water from the system.

It is clear, therefore, that the results obtained in this investigation do not permit of a simple explanation; they demonstrate, however, the complexity of the changes which accompany the dissolution of substances in water.

#### XLVIII.—*The Phosphoric Acids.*

By ALFRED HOLT and JAMES ECKERSLEY MYERS.

THE molecular constitution of ortho-, pyro-, and meta-phosphoric acids and the conversion of one into another have been the subjects of many investigations and differences of opinion.

Graham (*Phil. Trans.*, 1833, **52**, 253) by qualitative tests showed the existence of the three varieties of phosphoric acid, and concluded that "the other modifications (meta- and pyro-) pass directly into the condition of this acid (ortho-) on keeping their aqueous solutions for some days or more rapidly on boiling."

Sabatier (*Compt. rend.*, 1888, **106**, 63), by titrating solutions of the meta-acid of different strengths at regular intervals and using

various indicators, concluded that the meta-passes directly into the ortho-variety without the formation of pyro-acid, or at least with the formation of only a trace of it at first, the rate of change being accelerated by concentration and by heat. In further communications (*ibid.*, 1889, **108**, 738, 804), he assumes, with Fleitmann and Henneberg, the existence of complex molecules of the meta-acid, and finds that the rate of change is accelerated by the addition of sulphuric and hydrochloric acids, whilst it is retarded by acetic acid.

Blake (*Amer. Chem. J.*, 1902, **27**, 68), by measurements of the rate of change of the refractive index, concluded that a 10*N*-solution of the meta-acid was completely hydrated in four days.

The results of the investigations of Berthelot and André (*Compt. rend.*, 1896, **123**, 776; 1897, **124**, 265), Giran (*Ann. Chim. Phys.*, 1903, [vii], **30**, 203), and Tanatar (*J. Russ. Phys. Chem. Soc.*, 1898, **30**, 99) have been summarised in a paper by Balareff (*Zeitsch. anorg. Chem.*, 1910, **68**, 288), wherein he concludes that their experimental methods, and consequently their conclusion (that pyro-acid is formed as an intermediate substance) are open to criticism. In this paper, Balareff, by an analytical method based on the formation of cadmium or copper pyrophosphate, concludes that the meta-acid passes by hydration directly into the ortho-variety. In a previous paper (*Zeitsch. anorg. Chem.*, 1910, **67**, 234) he showed that whilst at moderate temperatures the dehydration of the ortho-acid produces pyro- and then meta-, at very high temperatures the change from ortho- to meta- should be direct. He did not, however, realise the latter condition experimentally.

Tilden and Barnett (*Trans.*, 1896, **69**, 158) have shown by vapour-density determinations that the molecule of metaphosphoric acid when in the state of vapour is not simple, but is a bimolecular complex, which at a very high temperature shows signs of dissociation. The experiments described at the end of the present communication confirm their observations on the complexity of the molecule.

It appears from the results of the above-mentioned authors that the question of the intermediate formation of pyrophosphoric acid during the hydration of the meta-variety is still unsettled, and, further, that there is uncertainty as to the molecular condition of the three varieties of phosphoric acid in solution.

Our experiments were first directed towards a study of the changes in the depression of the freezing point which a solution of the meta-acid undergoes on keeping, and also the direct estimation of the amount of meta-acid present in such a solution from time to time. Two solutions, the strengths of which were approximately

*N*- and 2*N*-metaphosphoric acid, were used. The following table gives the depression at varying intervals of time:

TABLE I.

Time (in days).	Depression of f. p.	
	<i>N</i> -Solution.	2 <i>N</i> -Solution.
0	0.697	1.452
2	0.900	1.900
5	1.100	2.485
7	1.203	2.685
10	1.305	2.895
12	1.425	3.150

It will be seen from the above values that the depressions recorded for the 2*N*-solution are slightly more than double those for the *N*-solution, so that it follows, that whatever the nature of the change which is taking place may be, increasing the strength of the solution from *N* to 2*N* does not materially affect the velocity.

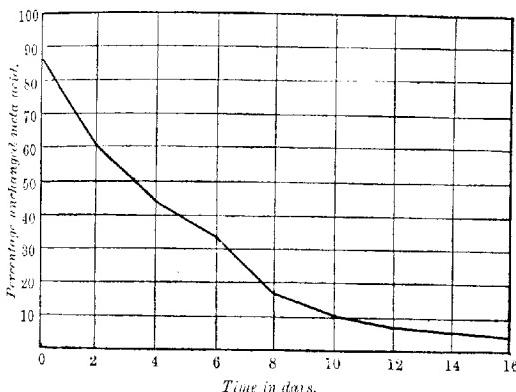
In order to determine the rate at which the hydration took place, the amount of unchanged meta-acid in the solution was estimated from day to day by precipitation with barium chloride. This method was adopted only after numerous trials with other reagents, but preliminary experiments led us to conclude that it was quite trustworthy. When barium chloride is added in large excess to a solution containing ortho-, pyro-, and meta-phosphoric acids, a precipitate is obtained, which, when washed and dried at 100°, was found to have a composition represented by the empirical formula  $\text{Ba}(\text{PO}_3)_2$ . A large number of samples of this precipitate were prepared and analysed by decomposition with nitric acid, the barium being subsequently estimated as sulphate, and they were found to have a practically constant composition. To test the method still further, a solution of the meta-acid, which had been kept for some time, was precipitated with largely varying amounts of barium chloride, the smallest amount being a slight excess. When the same volumes of the acid solution were taken, the weight of the precipitate obtained did not materially vary. A solution of meta-acid of about normal strength was prepared, and a portion of it precipitated with barium chloride from time to time. The amount of unchanged meta-acid could therefore be calculated, and the values in the following table were obtained:

TABLE II.

Time (hours).	Unchanged		Water in gram-mols.	$K_1$	$K_2$
	meta-acid,	meta-acid in			
0	84.92	0.829	55.53	—	—
46	60.80	0.518	55.22	0.0045	0.0043
99	44.35	0.378	55.03	0.0053	0.0035
142	31.87	0.270	54.97	0.0036	0.0034
190	17.63	0.150	54.85	0.0053	0.0053
238	10.28	0.088	54.79	0.0048	0.0048
287	6.61	0.056	54.76	0.0039	0.0040
382	4.55	0.039	54.74	0.0017	0.0016

The fresh solution contained 0.852 gram-molecule of meta-phosphoric acid, but 15 per cent. of it had changed before the measurements were begun.

An examination of the above table shows, in the first place, that



the values for the percentage of unchanged meta-acid in the solution do not fall on a regular curve, the rate of decrease becoming markedly accelerated after the solution has been kept for about 140 hours. These values are shown for the sake of clearness on the annexed curve. Further, from the values of  $K_1$  and  $K_2$ , which represent the velocities of the reaction calculated for a unimolecular and bimolecular change respectively, it is evident that the hydration of the meta-acid does not take place according to any simple scheme.

As further evidence on this point, the freezing points of a solution of the same strength as that employed for the determination of the meta-acid by precipitation with barium chloride were determined,

and the theoretical values were calculated on the assumption that the acid changed directly into the ortho-variety, dissociation being of a negligible amount. (The latter conclusion is justified by conductivity measurements.)

TABLE III.

Time (hours).	Unchanged $\text{HPO}_3$ in 100 c.c. solution, as $\text{H}_3\text{PO}_4$ in 100 c.c. solution.	Converted $\text{HPO}_3$ calc. Depression due to un- changed $\text{HPO}_3$ calc.	<i>A.</i> Depression due to un- changed $\text{HPO}_3$ calc. for simple mols.	<i>B.</i> Depression due to un- changed $\text{HPO}_3$ calc. for double mols.	<i>C.</i> Depression due to un- changed $\text{HPO}_3$ calc. for triple mols.	<i>D.</i> Depression due to changed $\text{HPO}_3$ calc. as $\text{H}_3\text{PO}_4$ .	Observed depression.			
							<i>A</i> + <i>D.</i>	<i>B</i> + <i>D.</i>	<i>C</i> + <i>D.</i>	
0	6.64	0.21	1.544	0.772	0.515	0.039	1.583	0.811	0.554	0.907
46	4.14	3.26	0.963	0.481	0.321	0.619	1.582	1.100	0.940	0.969
99	3.02	4.64	0.702	0.351	0.234	0.880	1.582	1.231	1.214	1.649
142	2.17	5.69	0.504	0.252	0.168	1.080	1.584	1.332	1.248	1.179
190	1.20	6.87	0.279	0.139	0.099	1.305	1.584	1.444	1.404	1.249
238	0.70	7.48	0.163	0.081	0.054	1.420	1.583	1.501	1.474	1.395
287	0.45	7.79	0.105	0.052	0.035	1.479	1.584	1.531	1.514	1.429
382	0.31	7.96	0.072	0.036	0.024	1.511	1.583	1.547	1.535	1.501

Table III contains these results. It will be noticed that the freezing point of the almost fresh solution gives a depression corresponding with a molecular weight for the meta-acid of between  $(\text{HPO}_3)_2$  and  $(\text{HPO}_3)_3$ , and it has subsequently been shown that this abnormal value does not arise from ionisation, but is undoubtedly due to the presence of complex molecules. The depression has therefore been calculated for the unchanged meta-acid on the assumption that it is present (*a*) in simple molecules, (*b*) in double molecules, and (*c*) in triple molecules. The experimentally determined values in the last column show that the hydration of the meta-acid does not proceed according to the equation  $\text{HPO}_3 + \text{H}_2\text{O} = \text{H}_3\text{PO}_4$ , but that at the commencement of the reaction at any rate, the molecules of the meta-acid are complex. From these values it is neither possible to say whether pyro-acid is formed as an intermediate compound, nor whether the complex molecules of the meta-acid first break down and subsequently become hydrated.

Although it has not been found possible to estimate either the pyro- or ortho-acids quantitatively in a mixture of all three varieties, the presence of the pyro-acid has been shown qualitatively by the following method. A solution of the meta-acid which had been kept about a fortnight was neutralised with sodium hydroxide, using phenolphthalein as indicator, and the resulting liquid fractionally precipitated with silver nitrate. At first, the yellow precipitate of silver ortho-phosphate was obtained. This was filtered off, and more

silver nitrate added. By repeating this process, a white precipitate formed, which gradually became yellow. By filtering it off immediately, it was found possible to obtain it absolutely colourless. If the neutralised solution be acidified by a small quantity of dilute nitric acid and then precipitated with silver nitrate, a colourless precipitate is obtained at once, owing to the differing solubility of the silver precipitates in nitric acid.

The white precipitate was washed and dissolved in nitric acid, and the silver precipitated with hydrochloric acid. The resulting acid solution did not coagulate albumen, although a trace of the meta-acid added to it at once brought about this change.

This process was frequently repeated with solutions of meta-phosphoric acid which had been kept some time, and always with the same result, so that it must be concluded that the pyro-acid is formed by the action of water on the meta-variety. This confirms the views of Berthelot and André, but is not in accordance with the results of Sabatier and Balaresh.

Since orthophosphoric acid on dehydration yields first pyro- and then meta-acid, it follows that on hydration the reverse change should occur. The results of Berthelot and André show that the change from meta- to pyro- proceeds more rapidly than that from pyro- to ortho-, and as the experimental method of Sabatier does not satisfactorily distinguish between pyro- and ortho-acids, the absence of pyro-acid recorded by various authors might arise from one change taking place too fast for observation.

The concentration of the solution will also have its effect. The more dilute it becomes, the faster one would expect the final state to be reached, unless the reaction is truly bimolecular, in which case the greatest velocity would be when the two reacting substances were present in equal concentration. It is therefore possible that the reason we have observed the presence of pyro-acid during the hydration is that our solutions were of a strength particularly favourable to its formation.

From the experiments already described, we were led to examine each of the phosphoric acids separately.

Pure crystalline ortho-acid, when dissolved in water, gave a depression of the freezing point concordant with a molecular weight of 93 (theory 98). Conductivity experiments showed the acid to be very slightly ionised, and it may therefore be concluded that the undissociated molecules in solution are represented by the formula  $H_3PO_4$ .

A few attempts were made to measure the vapour pressure of this acid during dehydration, but the results were inconclusive. Although the pyro- and meta-acids are readily formed from it, no

sudden change in the vapour pressure was detected, such as one would expect when one compound changed into another. It would seem that molecular compounds are probably formed during the dehydration, a conclusion to which Balareff also inclines.

Two varieties of pyrophosphoric acid have been examined. One was a viscid, syrupy liquid obtained by dehydrating the ortho-acid, and the other was obtained in aqueous solution by decomposing lead pyrophosphate by hydrogen sulphide. An approximately normal solution of the syrupy variety gave a depression of the freezing point, which indicated the presence of complex molecules of the acid of composition between  $(H_4P_2O_7)_4$  and  $(H_4P_2O_7)_5$ , whereas in the solution obtained from the lead salt the molecules appeared to be simple. Conductivity measurements again showed little ionisation, so that it may be concluded that very complex molecules, whether associated or not with molecular compounds, are formed by dehydrating the ortho-acid.

The syrupy solution, on keeping for some time, became a mass of crystals, which gave qualitative tests for both ortho- and pyro-acids, so that in this condition the pyro-acid cannot be regarded as a stable substance.

Four varieties of metaphosphoric acid, differing either in physical characters or molecular condition in solution, have been examined. Very little ionisation is found to take place in dilute aqueous solutions, and the differences between them are almost certainly the result of polymerisation into molecules of varying complexity.

The first variety is obtained by heating to redness for a short time sticks of pure glacial phosphoric acid. As thus obtained, it is a vitreous solid, deliquescent in moist air, and readily soluble in water. Freezing-point determinations of its solution indicate the presence of molecules of composition  $(HPO_3)_3$ , the values not varying greatly for solutions of strength 2*N* or *N*/10.

When sodium metaphosphate glass is dissolved in water, a depression of the freezing point is obtained, which gives a molecular weight of 314, the theoretical value for  $(NaPO_3)_3$  being 306. It appears therefore that not only the acid, but its alkaline salts, can exist in solution in termolecular complexes.

The second variety is obtained by heating the previous glassy solid to redness for several hours. It is a hard and brittle glass, having a sp. gr. of 2.488. It becomes sticky in moist air, but not so readily as the former variety. When a fragment of this glass is put into water a curious phenomenon, first recorded by Sabatier, takes place. Although a portion seems to dissolve directly, by far the larger amount of the substance is gradually shot off as minute particles into the surrounding water with a sharp, crackling sound,

and the liquid becomes turbid through their presence, solution taking place slowly. When a fragment of this glass is placed in water and viewed microscopically, the particles are seen to be clear fragments with typical glassy fracture. They are expelled with considerable velocity, but as the solution in the immediate neighbourhood of the fragment becomes saturated with the acid, they are formed in constantly decreasing amount.

When this "crackling" variety of the meta-acid is heated for a long time (about twenty-four hours) at a dull red heat, its characters are found to be changed. Although still a hard and brittle glass, its specific gravity has somewhat diminished (2·216), and it is almost insoluble in water. A portion of this glass has been kept in the laboratory for many days without becoming sticky, and when ground to the finest powder takes several days to dissolve in water. No crackling is heard during solution, and no particles are shot off the mass of the glass. Freezing-point determinations show the presence of bimolecular complexes ( $\text{HPO}_3$ )<sub>2</sub>.

When lead metaphosphate is decomposed with hydrogen sulphide, a solution of metaphosphoric acid is obtained, which apparently contains simple molecules of the acid ( $\text{HPO}_3$ ), since freezing-point determinations give a molecular weight of 102 (theory 80), and the acid is slightly ionised.

These experiments on each of the phosphoric acids show that solutions containing simple molecules can be obtained by decomposing the lead salts, the acids prepared by the dehydration of the ortho-variety invariably containing more or less complex molecules.

The decomposition of a meta- or pyro-salt might be expected to yield simple molecules of the acids, whilst the dehydration of the ortho-acid, since it does not proceed strictly in two stages, would favour the formation of molecular complexes.

The following conclusions may be drawn from the experiments described in this paper:

1. Pyrophosphoric acid is formed as an intermediate compound during the hydration of metaphosphoric acid.
2. The rate of hydration does not accord with any simple order of reaction.
3. Meta and pyro-phosphoric acids, when prepared by dehydrating the ortho-variety, give complex molecules in solution, but when prepared by decomposing the corresponding lead salts, simpler molecules result.

THE UNIVERSITY,  
MANCHESTER.

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XLIX.—*The Determination of Solubility Coefficients by Aspiration.*

By WILLIAM JACOB JONES (Fellow of the University of Wales).

It is well-known that a given volume of air aspirated at a sufficiently slow rate through a solution of a gas in a liquid—provided Dalton's law is obeyed—abstracts and carries along with it an amount of the gas which is proportional to the concentration of the solution. Methods based on this fact have been applied to the following problems: (1) to determine the partial pressure of volatile substances in solution (Gahl, *Zeitsch. physikal. Chem.*, 1900, **33**, 178); (2) to compare the relative influence of different salts on the solubility of gases in aqueous solution (McLauchlan, *Zeitsch. physikal. Chem.*, 1903, **44**, 600; Gaus, *Zeitsch. anorg. Chem.*, 1900, **25**, 236; Konowaloff, *J. Russ. Phys. Chem. Soc.*, 1899, **31**, 910; Abegg und Riesenfeld, *Zeitsch. physikal. Chem.*, 1902, **40**, 84); (3) to determine the amount of gas in the dissolved state set free in homogeneous equilibria (Jakowkin, *Zeitsch. physikal. Chem.*, 1899, **29**, 626; Orton and Jones, *Trans.*, 1909, **95**, 1456).

On the assumption that the laws of Dalton and Henry hold, a very clear theoretical treatment of the relation between the rates of evasion and of invasion of a gas from and into a liquid respectively, and the solubility of the gas in the liquid, has been given by Bohr (*Ann. Physik*, 1897, [iii], **62**, 644; 1899, **68**, 500). He experimented with solutions of carbon dioxide in water and in sodium chloride solutions. He considers that when a rapid current of an inert gas free from carbon dioxide is passed over a well-stirred solution of carbon dioxide, the time-rate of escape (or "evasion") of the latter gas from solution is proportional to the concentration of the solution and to its exposed surface. From the mathematical expression of this assumption he obtains an "evasion coefficient,"  $\beta$ , which denotes the volume of carbon dioxide (at N.T.P.) escaping per minute through 1 sq. cm. of exposed surface, into an atmosphere free from that gas, from a solution containing 1 c.c. (at N.T.P.) in 1 c.c. of the solution. In a similar way he defines the "invasion coefficient,"  $\gamma$ , of carbon dioxide into water as the volume of that gas which, under a pressure of 760 mm. of mercury, enters through 1 sq. cm. of surface per minute into well-stirred water free from carbon dioxide. If  $\alpha$  denotes the absorption coefficient of carbon dioxide in water, it is easily seen that  $\gamma = \alpha\beta$ . Bohr determined  $\alpha$  by abstracting the gas from its saturated solution by means of a Hagen pump, and measuring the volume of gas. He determined  $\gamma$

both experimentally and by substituting the values he had found for  $\alpha$  and  $\beta$  in this formula. The comparison does not show a very good agreement between the calculated and found values of  $\gamma$ .

Perman has made very extensive use of aspiration methods of experiment, applying them to the following determinations: (1) the rate of escape of ammonia from the aqueous solution when a uniform current of air is bubbled through it (*Trans.*, 1895, **67**, 368, 983; 1898, **73**, 511)—he shows that the amount of ammonia,  $q$ , present in the solution when a volume,  $V$ , of air has been drawn through is represented by the equation  $\log q = a + b \cdot V$ ,  $a$  and  $b$  being constants for a given experiment; (2) the vapour pressure of water and the partial pressure of ammonia in its aqueous solutions (*Trans.*, 1901, **79**, 718; 1903, **83**, 1168; *Proc. Roy. Soc.*, 1903, **72**, 72). He has also made a careful study of the sources of error of the method (*J. Physical Chem.*, 1905, **9**, 36; *Proc. Roy. Soc.*, 1905, **76**, 1, 174).

Steele (*Trans.*, 1903, **83**, 1470) assumes that "the desaturation of a saturated solution of hydrogen chloride in toluene by a steady current of hydrogen follows the course of a unimolecular reaction, namely:

$$K = \frac{1}{T} \log_e \frac{a}{a - x},$$

where  $a$  denotes the amount of gas contained in the saturated solution, and  $x$  the amount carried away in the time  $T$ ."

When the molecular condition of a substance is the same in two phases, it divides itself between them, so that the ratio of its concentration in one phase to its concentration in the other phase is always a constant (the Partition Law). On this law as basis, Ostwald defines the solubility coefficient of a gas in a liquid as the ratio, when equilibrium has been established, of the concentration of the gaseous solute (in gram-molecules per unit volume) in the liquid phase to its concentration in the vapour phase in contact with the former phase; otherwise expressed:

$$\text{Solubility coefficient} = \frac{\text{Concentration in the liquid phase}}{\text{Concentration in the vapour phase}}$$

In this paper it is shown that solubility coefficients of volatile solutes, provided the system obeys the laws of Dalton and Henry, can be determined from the amount of solute which is carried away by an inert gas when known volumes are bubbled through solutions of known strength and volume.

Let a volume  $V$  c.c. of an inert gas be drawn at a very slow rate and in very minute bubbles through a volume  $v$  c.c. of a well-stirred solution of a volatile substance maintained at a constant temperature; if  $s$  denote the solubility coefficient,  $\alpha$  the amount of

volatile solute initially, and  $b$  the amount finally, present in the solution, then it can be shown that

$$s = \frac{V}{v \cdot \log_e \frac{a}{b}}.$$

Evidently  $(a - b)$  denotes the amount of solute abstracted by the inert gas.

In order to establish this relation, consider an instant when a volume  $x$  c.c. of inert gas has been bubbled through. At this instant let the amount of volatile solute in the solution be  $y$  gram or  $y$  gram-molecules; let a small additional volume  $\delta x$  of inert gas be drawn through, and let it abstract a small amount  $\delta y$  of solute from the solution. Then, provided the solution is well stirred and the inert gas is in the form of very small bubbles and drawn through at such a rate that the solute is allowed sufficient time to attain at each instant its maximum partial pressure in the abstracting gas (which takes the less time to accomplish the more minute the bubbles), it follows from the definition that

$$s = \frac{\frac{y}{v}}{\frac{\delta y}{\delta x}}.$$

and, in the limit,

$$\frac{dy}{dx} = \frac{y}{v \cdot s}.$$

Since, as  $x$  increases,  $y$  diminishes, we may change the sign of the right-hand side, and on integration between the limits,  $x=0$ ,  $y=a$  and  $x=1$ ,  $y=b$ , we obtain:

$$s = \frac{V}{v \cdot \log_e \frac{a}{b}}.$$

From this equation, we can at once draw the following deductions:

(1) When such a small volume of abstracting gas is employed that only a small quantity of solute is removed,  $s$  is given by the obvious relation (*Jakowkin, loc. cit.*):

$$\frac{1}{s} = \frac{\frac{(a-b)}{V}}{\frac{a}{v}},$$

for:

$$\frac{1}{s} = \frac{v}{V} \cdot \log_e \frac{a}{b} = \frac{v}{V} \cdot \log_e \left( 1 + \frac{a-b}{b} \right).$$

On expanding the logarithm factor in series, and neglecting the

square and higher powers of the small quantity  $(a-b)/b$ , we obtain:

$$\frac{1}{s} = \frac{v \cdot (a-b)}{V \cdot b} = \frac{v \cdot (a-b)}{V \cdot a}$$

approximately.

(2) The logarithmic law found empirically by Perman (*loc. cit.*) for the rate of loss of ammonia by a solution through which a steady current of air is being aspirated follows thus:

$$\log a - \log b = \frac{V}{s \cdot v}$$

In a given experiment,  $s$ ,  $v$ , and  $\log a$  are all constant, and  $b$  denotes the amount of gas in solution after a volume  $V$  of air has been bubbled through:

$$\therefore \log b = - \frac{V}{s \cdot v} + \log a$$

(compare Perman, *loc. cit.*)

$$\log b = b \cdot V + a.$$

(3) An explanation of the direct proportionality between the amount of solute carried away by a given volume of abstracting gas and the strength of the solution (Orton and Jones, *loc. cit.*, p. 1463) is furnished by this equation, for in such a series of experiments,

$$v_1 = v_2 = v_3 = \dots; \text{ and } V_1 = V_2 = V_3 = \dots$$

Whence

$$\log \frac{a_1}{b_1} = \log \frac{a_2}{b_2} = \dots$$

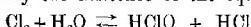
$$\therefore \frac{a_1}{b_1} = \frac{a_2}{b_2} = \dots$$

and

$$\frac{a_1 - b_1}{a_1} = \frac{a_2 - b_2}{a_2} = \dots$$

that is, the amount of solute carried away by the inert gas is proportional to the initial concentration of the solution (see Fig. 3).

This relation affords a means of testing whether the volatile solute-solvent system obeys the laws of Dalton and Henry or not. For this purpose a number of experiments are carried out, using solutions varying in strength from the most dilute up to the saturated solution. If this proportionality holds throughout that range, then these laws are followed. By this means it was found that deflection arose in the case of dilute chlorine solutions in water, showing clearly the existence of the equilibrium:



investigated by Jakowkin (*loc. cit.*) (see table VI and Fig. 2).

The value of

$$\frac{V}{v \log_e \frac{a'}{b'}}$$

which, if this equilibrium did not exist, would be constant, increases with dilution.

In the case of bromine water, the corresponding formation of hypobromous acid and hydrobromic acid is very much less extensive (see table IX) (compare Bray, *J. Amer. Soc.*, 1910, **32**, 932).

Provided an accurate knowledge of each of the quantities,  $a$ ,  $b$ ,  $V$ , and  $v$ , is possible, the formula:

$$s = \frac{V}{v \cdot \log_e \frac{a}{b}}$$

furnishes a means of experimentally determining solubility coefficients. In the following section it is shown how this can be accomplished. It is more practicable to take for the value of  $b$  the difference between the value of  $a$ , which is accurately determined, and the amount of solute which is carried away by the abstracting gas—this being trapped by suitable means and accurately estimated—than by direct estimation. The accurate value obtained in this way is roughly checked by the analysis of an aliquot portion of the solution at the end of the aspiration.

It will be noticed that the solubility coefficient can be determined by this method without the necessity of preparing a saturated solution.

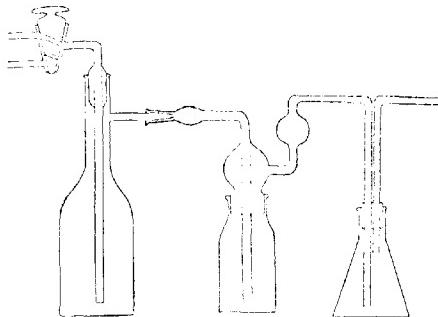
#### EXPERIMENTAL.

Experiments in verification of the preceding theorem were carried out with chlorine and bromine solutions in carbon tetrachloride, in acetic anhydride, in acetic acid, in water, and in aqueous acetic acid.

The apparatus consisted of a bubbler containing the solution, followed by small wash-bottles containing potassium iodide solution, and finally the aspirator, the whole being immersed in a constant temperature bath. The bubbler and the potassium iodide wash-bottles are shown in Fig. 1. They were designed by Professor Orton. The leading tubes were of capillary tubing, and passed through a solid glass stopper. By this means the waste dead space above the solution was reduced to a minimum, the bubbler being as nearly as possible full of solution. On the tube connecting this vessel with the first potassium iodide wash-bottle, a small bulb had been blown, and this was packed with glass-wool, which, experiment showed, completely removed all spray from the air. This

potassium iodide wash-bottle was attached by means of a well-ground glass joint. It was followed by a second wash-bottle, also containing potassium iodide solution; this, however, was not necessary except where the halogen solution was very concentrated, absorption being complete in the first wash-bottle. Titration of the iodine set free in these wash-bottles gives the amount of chlorine or bromine carried away by the air ( $-[a - b]$ ). The solutions were prepared from dry chlorine and bromine in glass-stoppered vessels, and transferred, without exposure to the air, to a standard burette, from which a portion of the solution was delivered into potassium iodide solution and a known volume (c.c.) poured into the bubbler so as to fill it as completely as possible. Titration of the iodine set free from the potassium iodide served to give the amount ( $a$ ) of

FIG. 1.



halogen introduced into the bubbler. It was found that with care the loss of chlorine and bromine during this transference was very small, and it is doubtful whether a greater accuracy could have been attained by preparing the solutions *in situ* in the bubbler. In some of the later experiments (tables IV, V, VI, IX, XII),  $a$  was determined in a different way, thus: a known volume of solution was introduced into the bubbler, and by means of a standard pipette, 2 c.c. of the solution were withdrawn and poured into potassium iodide solution. When the solution had acquired the temperature of the bath, a current of air, freed from dust and water vapour, saturated with the vapour of the solvent, and maintained at the temperature of the experiment by being drawn through the apparatus in the bath, was bubbled through the solution. Efficient stirring was ensured by the narrow form of the bubbler and the minuteness of the bubbles. Trials showed that

under the conditions of the experiments there was no difference in the amount of chlorine carried over when 250 c.c. of air were bubbled through in times varying from one and a-quarter to fifty-one minutes. The volume ( $V$ ) of air aspirated through the solution was determined by measuring the volume of liquid displaced in the aspirator by syphoning it over into graduated flasks. In experiments of accuracy, in order to ensure that the air measured in the aspirator was as nearly as possible under the same conditions—especially as regards volume—as the air aspirated through the solution, it would be necessary to fix a calcium chloride drying-tube following the last potassium iodide wash-bottle in order to remove the aqueous vapour and to fill the aspirator with the pure solvent, thereby reducing the air to exactly the same condition as it was in when passing through the solution. For the same reason it is necessary that the air should not at any time during its passage through the apparatus bubble through any considerable depth of liquid between the bubbler and the aspirator, which for this purpose should be as squat in form as possible. The air, which passes through the solution in the form of spherical bubbles, is collected in the aspirator above the plane surface of the liquid. Now the pressure inside a spherical bubble of radius  $r$  exceeds the pressure outside by  $2T/r$ , where  $T$  denotes the surface tension. Hence, in order to avoid having to make a correction owing to surface tension, it is necessary that the bubbles should not be too minute. The total error in the measurement of  $V$ , made by assuming the volume of liquid syphoned from the aspirator to be equal to the sum of the volumes of the bubbles of air as they passed through the solution, in consequence of these sources of error was less than 0·2 c.c. per 100 c.c.

Titration of iodine set free were carried out with  $N/50$ -sodium thiosulphate solution delivered from a standard 10 c.c. burette graduated in 0·02 c.c. In the tables the titres have been reduced to  $N/10$ .

The solutions were shielded from light, and the experiments were carried out in a darkened room.

Special attention was given to the purity of all chemicals used. The specially purified acetic acid was partly prepared in this laboratory, and partly obtained from Kahlbaum. The carbon tetrachloride was redistilled several times. The bromine was washed with water, dried with sulphuric acid, and distilled from a few crystals of potassium bromide. Kahlbaum's acetic anhydride was used without further purification.

By the term "75 per cent. acetic acid" is meant a solution prepared by mixing 75 volumes of glacial acetic acid with 25 volumes

of pure redistilled water, and similarly with acetic acids of other concentrations.

TABLE I.

Chlorine in Carbon Tetrachloride. Temperature 15°.

v.	V.	Time occupied in aspiration, minutes.	(a - b).	a.	<i>b.</i>		s.
					Calc.	Found.	
95.0	436.0	13	3.85	47.01	43.16	42.92	53.7
95.0	430.0	5	3.22	33.27	35.05	35.00	51.4
95.0	297.0	3	3.93	65.35	61.62	61.05	51.0
95.0	298.0	4	0.75	12.55	11.80	11.57	50.7
							51.7

TABLE II.

Chlorine in 99.84 per cent. [0.16 per cent. water] Acetic Acid.  
Temperature 15°.

95.0	250.0	2.5	3.68	53.30	49.62	49.20	36.9
95.0	250.0	2.5	1.99	28.70	28.71	26.50	36.6
95.0	250.0	2.5	5.10	53.00	67.90	66.80	36.4
95.0	250.0	8.3	2.18	31.70	29.52	29.32	36.9

TABLE III.

Chlorine in 90 per cent. Aqueous Acetic Acid. Temperature 15°.

95.0	250.0	2.5	2.53	26.41	23.88	—	26.1
95.0	250.0	2.5	12.83	128.8	116.0	—	25.1
95.0	250.0	2.5	6.01	59.09	53.05	—	24.4
95.0	250.0	2.5	2.41	24.40	22.0	—	25.4

25.3

TABLE IV.

Chlorine in 75 per cent. Aqueous Acetic Acid. Temperature 15°.

v.	V.	Time occupied in aspiration, minutes.	(a - b).	a.	<i>b.</i>		s.
					Calc.	Found.	
104.0	250.0	4.8	3.22	24.34	16.39	16.39	
104.0	250.0	5.0	8.66	63.42	16.39	16.39	
104.0	250.0	4.8	10.79	79.57	16.50	16.50	
							16.43

TABLE V.

Chlorine in 65 per cent. Aqueous Acetic Acid. Temperature 15°.

104.0	250.0	4.8	3.99	25.06	13.88	
104.0	250.0	4.5	6.62	89.54	13.10	
104.0	250.0	4.5	14.04	85.30	13.36	

13.43

TABLE VI (see Fig. 2).  
Chlorine in Water. Temperature 15°.

<i>r.</i>	<i>V.</i>	Time occupied in aspiration, minutes.	Time occupied in aspiration,		$\frac{V}{r \cdot \log \frac{a}{b}}$
			( <i>a</i> - <i>b</i> )	<i>a.</i>	
104.0	100.0	7.0	33.44	250.3	6.7
104.0	100.0	7.0	20.65	177.5	7.7
104.0	100.0	7.0	11.92	133.0	8.4
104.0	100.0	7.0	11.19	112.1	9.1
104.0	100.0	7.0	9.687	110.4	10.4
104.0	100.0	7.0	6.146	76.78	11.5
104.0	105.9	7.3	1.199	28.66	22.5
104.0	100.0	7.0	0.514	19.21	35.5
104.0	100.0	7.0	0.0077	4.207	524.8

FIG. 2 (see Table VI).

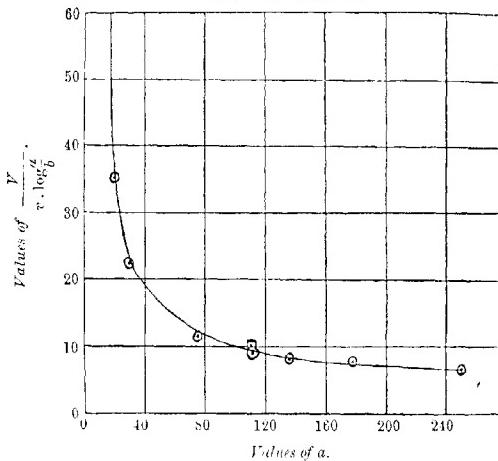


TABLE VII.

Bromine in 90 per cent. Aqueous Acetic Acid. Temperature 15°.

<i>r.</i>	<i>V.</i>	Time occupied in aspiration, minutes.	<i>a.</i>	<i>b.</i>	
				Calc.	Found.
95.0	1000	30	3.02	157.32	154.9
95.0	1000	10	1.23	64.60	62.96
95.0	1000	10	1.19	64.03	62.63
95.0	1000	10	2.05	105.72	103.15
					551

TABLE VIII.

Bromine in 25 per cent. Aqueous Acetic Acid. Temperature 15°.

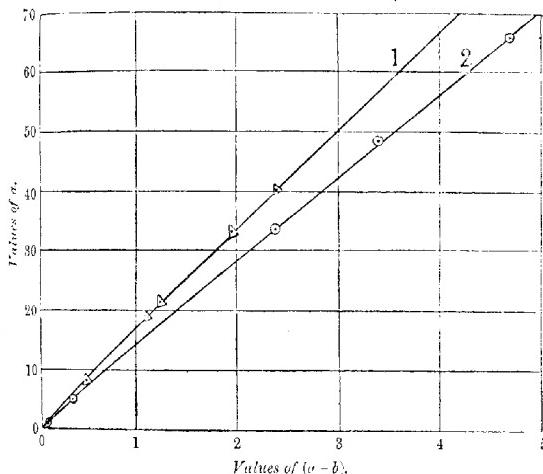
124	500	12	5.88	68.70	62.82	62.92	54
133	500	12	2.78	34.35	31.57	31.20	57
							56

TABLE IX (see Curve 2, Fig. 3).

Bromine in Water. Temperature 15°.

<i>r.</i>	<i>V.</i>	Time occupied in aspiration, ( <i>a</i> - <i>b</i> ), minutes.	<i>a.</i>	<i>s.</i>	Time occupied in aspiration, ( <i>a</i> - <i>b</i> ), minutes.	
					<i>a.</i>	<i>s.</i>
104.0	500	12	9.17	66.37	32.3	
101.0	250	6	4.70	65.97	32.5	
104.0	250	10	3.382	48.63	33.4	
101.0	250	6	2.30	33.00	33.2	
101.0	250	10	0.357	5.211	33.9	
104.0	250	10	0.075	1.267	39.4	

FIG. 3 (see Tables IX and XII.).



When *s* has been determined by experiments similar to the preceding for a given volatile substance in a medium, the concentration of the volatile substance existing in the free state in solution in homogeneous equilibria in the medium may be determined by aspiration experiments, for

$$\log \frac{a}{b} = \frac{V}{v \cdot s} \dots \dots \dots \quad (1)$$

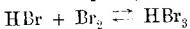
and  $a - b =$  amount of volatile solute carried over by  $V$  c.c. of inert gas from  $v$  c.c. of solution . . . . . (2).

Solving these two equations, we obtain  $a$ , the concentration of the dissolved volatile substance. In order to disturb the equilibrium as little as possible, it is essential that the amount of solute extracted from the solution by the inert gas should be no more than is necessary for accurate analysis.

As an illustration of this application may be given the following investigation of the extent of combination of bromine and hydrogen bromide in water, in acetic acid, and in aqueous acetic acids. A considerable amount of work has been done on this subject in aqueous solution, both by methods based on extraction of the bromine by means of such liquids as carbon disulphide and carbon tetrachloride (Wildermaann, *Zeitsch. physikal. Chem.*, 1893, 11, 46; Roloff, *ibid.*, 1894, 18, 341; Jakowkin, *ibid.*, 1896, 20, 19), and by electrolytic methods (Boericke, *Zeitsch. Elektrochem.*, 1905, 11, 57). Measurements of velocities of bromination in aqueous solution always reveal an apparent loss of activity on the part of bromine with the progress of the reaction. This is due to the combination of the hydrogen bromide produced with the bromine to form hydrogen tribromide (Ramberg, *Zeitsch. physikal. Chem.*, 1900, 34, 561; Bruner, *ibid.*, 1902, 41, 513; Bugarszky, *ibid.*, 1901, 38, 561; 1904, 48, 63; Bognár, *ibid.*, 1910, 71, 529).

Bugarszky shows how the equilibrium constant:

$$K = \frac{[\text{HBr}][\text{Br}_2]}{[\text{HBr}_3]}$$



may be calculated from measurements of the speed of bromination of acetaldehyde. At  $25^\circ$  he obtains the value 0.0665 for  $K$ ; Jakowkin's value is 0.065.

The procedure in the present experiments was as follows. A known volume of standard hydrogen bromide solution was put in a flask in the bath. A solution of bromine in the solvent was standardised, and a known volume run in from a burette into the bubbler. So much solvent was added to the hydrogen bromide solution, that on mixing with the bromine solution a convenient volume of solution was obtained. When the solutions had acquired the temperature of the bath, the contents of the flask were poured into the bubbler, and the whole having been allowed to stand in order that equilibrium should be established, a known volume of air was aspirated through. By substituting the value of the amount of bromine carried over by the air in equation (2), the two equations on solution give the value of  $a$ , for example, the concentration of  $\text{Br}_2$  in the system.

As examples may be given the following two experiments:

TABLE X.

Medium.		50 per cent. acetic acid.	Water.
r .....	104	104	
I' .....	500	250	
Amount of $\text{Br}_2$ used in preparation per litre of solution, gram-mol. ....	0.0330	0.0316	
Amount of $\text{HBr}$ used in preparation per litre of solution, gram-mol. ....	0.0330	0.0316	
Time which elapsed between mixing and beginning of aspiration (minutes) ....	10	12	
Time occupied in aspiration (minutes) ....	13	6	
Titre of 10 c.c. solution at the end of the aspiration .....	6.531	5.950	
Titre of $\text{Br}_2$ carried away by air .....	1.130,	3.335,	
corresponding with a concentration of $\text{Br}_2$ (and $\text{HBr}$ ) .....	0.0172	0.0230	
concentration $\text{HBr}_2$ .....	0.0158	0.0086	
Value of $K$ .....	0.0187	0.961	

TABLE XI.

Medium.	Tempera- ture.	Gram-mols. used in preparation of 1 litre of solution.		Gram-mols. per litre in equilibrium.			$K$ .
		$\text{Br}'$ .	$\text{Br}_2$ .	$\text{Br}'$ .	$\text{Br}_2$ .	$\text{Br}'$ .	
Water.	15	0.0316	0.0316	0.0088	0.0230	0.0230	0.051
	15	0.0158	0.0158	0.0028	0.0130	0.0130	0.061
	15	0.0316	0.0316	0.0088	0.0228	0.0228	0.059
25 per cent. aqueous acetic acid.	15	0.0330	0.0330	0.0145	0.0185	0.0185	0.024
	15	0.0100	0.0070	0.0020	0.0050	0.0050	0.020
50 per cent. aqueous acetic acid.	15	0.0380	0.0330	0.0158	0.0172	0.0172	0.019
	16	0.0200	0.0200	0.0151	0.0049	0.0049	0.0016
99.6 per cent. acetic acid.	16	0.0400	0.0100	0.0290	0.0110	0.0110	0.0042
	16	0.0216	0.0122	0.0050	0.0042	0.0136	0.0071
	16	0.0225	0.0251	0.0142	0.0109	0.0083	0.0064
	16	0.1160	0.0559	0.0830	0.0129	0.0350	0.0051

Jakowkin obtained the value 0.065 for  $K$  for aqueous solutions at 25°.

The value of  $K$  increases with increasing dilution of the acetic acid, showing that the formation of perbromides is more extensive in concentrated acetic acid than in dilute acetic acid. The inconsistency in the value of  $K$  in glacial acetic acid solution may be due to incomplete ionisation of the tribromide or to an appreciable formation of higher perbromides. Steiner (*Ber.*, 1874, 7, 184), by the employment of low temperatures, isolated acetic acid hydrobromide perbromide from mixtures of bromine, hydrogen bromide, and glacial acetic acid, and, unless this compound undergoes complete thermal dissociation at 10°, it must interfere with the equilibrium.

In sharp contrast to the behaviour of bromine and hydrogen bromide, chlorine and hydrogen chloride do not combine to any appreciable extent. With as much as eight equivalents of hydrogen chloride to one of chlorine in glacial acetic acid solution, all the chlorine was found to be free. Table XII shows some similar experiments made with acetic anhydride solutions.

TABLE XII (see Curve 1, Fig. 3).

Chlorine in Acetic Anhydride. Temperature 15°.

a.	T. (minutes).	Time occupied in aspiration Hydrogen chloride.	Gram-mols. used in preparation per litre of solution.	Amount of chlorine expressed as the titre of 104 c.c. solution in c.c. N/10.		
				Chlorine.	a.	(a - b).
104.0	250.0	10	0.0000	0.01574	32.75	1.943 34.6
104.0	250.0	10	0.0000	0.01015	21.10	1.229 40.1
104.0	250.0	10	0.0000	0.00403	8.390	0.503 35.8
104.0	250.0	10	0.0293	0.01925	49.04	2.460 39.0
104.0	250.0	10	0.0353	0.00916	19.05	1.165 33.6
104.0	250.0	10				

The author is greatly indebted to Professor Orton, who suggested this investigation, for the interest he has taken therein, and for his kind help in designing the apparatus.

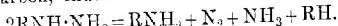
UNIVERSITY COLLEGE OF NORTH WALES,  
BANGOR.

### I.—The Auto-reduction of Hydrazines.

By FREDERICK DANIEL CHATTAWAY and MONTAGUE ALDRIDGE.

AROMATIC hydrazines, when heated, undergo simultaneous oxidation and reduction. As the precise course of any such auto-reduction depends only on the group to which the hydrazine concerned belongs, these interactions may be expressed by general equations.

Primary hydrazines yield a primary amine, nitrogen, ammonia, and a hydrocarbon, thus:



Unsymmetrical secondary hydrazines yield a secondary amine, nitrogen, and ammonia, thus:



Symmetrical secondary hydrazines yield a primary amine and an azo-compound, thus:



Many of these reactions go on slowly even at the ordinary temperature, the rate increasing rapidly as the boiling point of the hydrazine is approached. It is thus impossible to obtain any aromatic hydrazine quite pure by distillation, or to keep it so for an unlimited time, even when air is excluded.

When the hydrazines contain only unsubstituted hydrocarbon residues, the reactions are, as a rule, quantitative, but in the case of hydrazines containing substituted aromatic residues, although these primary decompositions take place to a considerable extent, other secondary reactions may also occur, especially at a high temperature, due to the presence of the substituted atoms or groups.

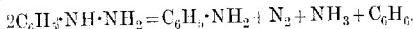
#### *Action of Heat on Phenylhydrazine.*

Emil Fischer, in his well-known paper describing the compound (*J. Annalen*, 1878, **190**, 81), noted that when phenylhydrazine was distilled under the ordinary pressure, a small quantity of ammonia was liberated. This he removed by exposing the freshly distilled liquid in a vacuum over sulphuric acid, but some years afterwards (*J. Annalen*, 1886, **236**, 198) he recommended that it should be distilled under diminished pressure to avoid this decomposition. Evidently this procedure, also, did not prove entirely satisfactory, for he later stated (*Ber.*, 1893, **26**, 19) that it is best obtained quite pure by frequently freezing it out from double its volume of ether at  $-10^{\circ}$ . Walter (*J. pr. Chem.*, 1896, [ii], **53**, 471) observed that phenylhydrazine, when heated in a sealed tube to  $300^{\circ}$  for three to four hours, decomposed into aniline, nitrogen, ammonia, and benzene, and Struthers (*Proc.*, 1905, **21**, 95) discovered that this action took place with almost explosive violence when small quantities of cuprous cyanide or cobalt cyanide were added to phenylhydrazine heated to near its boiling point.

It has, however, never been recognised that this reaction proceeds comparatively rapidly when phenylhydrazine is boiled, and that the liberation of ammonia which occurs when it is distilled is accompanied by the continuous evolution of nitrogen and formation of aniline, and, moreover, that the reaction is a characteristic general one of all primary aromatic hydrazines.

To investigate the reaction, 150 grams of pure phenylhydrazine, recently distilled under a pressure of 20 mm. and boiling constantly, were placed in a small, round-bottomed flask connected with a reversed condenser, through which steam was passed. The upper end of this was attached to a short upright condenser dipping into a flask, and the latter to a Volhard trap containing dilute hydrochloric acid. The exit tube from the trap dipped below the surface of water in a small pneumatic trough. The air contained in the

apparatus having been displaced by hydrogen, the phenylhydrazine was heated to gentle ebullition for about twelve hours. At first it boiled quietly at 241°. Ammonia and nitrogen were continually evolved, whilst benzene, which escaped condensation in the heated condenser, collected in the flask attached to the cooled condenser. After twelve hours' boiling, the residue in the flask was distilled and found to consist practically entirely of aniline. The nitrogen escaping was measured, and the ammonia weighed as ammonium chloride. The decomposition was thus shown to take place, within the limits of experimental error, quantitatively according to the equation:



This auto-reduction of phenylhydrazine takes place completely and instantaneously if the vapour of the compound is passed through a short length of hard glass tube packed with porous porcelain, and heated to a dull red heat in a furnace. The products are the same as when the decomposition is effected at the boiling temperature. Ammonia and nitrogen are liberated, whilst a mixture of aniline and benzene condenses. Small quantities of compounds boiling at a temperature higher than the boiling point of aniline are also present in the liquid condensing, formed doubtless by the action of heat on the benzene and aniline.

#### *Action of Heat on the Tolylyhydrazines.*

Fifty grams of *p*-tolylhydrazine were heated in the apparatus previously described, but with the steam-heated condenser replaced by a thin-walled glass tube filled with beads, and of such a length that when the liquid was gently boiling, only the toluene produced passed over into the second condenser.

*p*-Tolylhydrazine undergoes auto-reduction more easily than does phenylhydrazine, but in an exactly similar manner. It decomposes quantitatively into *p*-toluidine, nitrogen, ammonia, and toluene, thus:

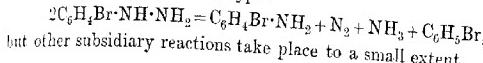


*o*-Tolylhydrazine behaves similarly to the *p*-compound, and yields *o*-toluidine, nitrogen, ammonia, and toluene.

#### *Action of Heat on p-Bromophenylhydrazine.*

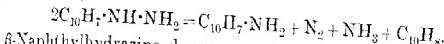
*p*-Bromophenylhydrazine at an elevated temperature decomposes much more easily than the unsubstituted phenylhydrazine. When heated above its melting point, bubbles of gas are given off between 115° and 120°. At about 140° the gas evolution becomes rapid,

nitrogen, ammonia, and bromobenzene are set free, and so much heat is evolved that even if the flame is removed the temperature quickly rises to about  $210^{\circ}$ , the action becoming violent. A brownish-black residue, which dissolves in alcohol to a blue liquid, is left in the distilling flask. On distilling, it yields considerable quantities of bromobenzene and *p*-bromoaniline. The main decomposition is of the usual primary hydrazine type:



#### *Action of Heat on the Naphthylhydrazines.*

When  $\alpha$ -naphthylhydrazine is heated above its melting point, bubbles of nitrogen and a little ammonia are given off at about  $120^{\circ}$ . As the temperature is raised, the evolution of gas increases, until at about  $240$ — $260^{\circ}$  it is very vigorous, ammonia and nitrogen being rapidly liberated, whilst naphthalene is set free. On distilling the solid residue, it is found to consist of a mixture of  $\alpha$ -naphthylamine and naphthalene. The decomposition takes place quantitatively, thus:

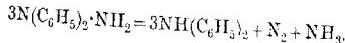


$\beta$ -Naphthylhydrazine decomposes similarly, but more easily. The liberation of ammonia is noticeable even at  $60^{\circ}$ , and at  $120^{\circ}$  bubbles of nitrogen form rapidly in the melted mass. The decomposition becomes, as before, more vigorous as the temperature rises to  $250^{\circ}$ . On distilling the residue after the evolution of gas has ceased, it is found to consist of  $\beta$ -naphthylamine and naphthalene.

Auto-reduction of the naphthylhydrazines goes on to an appreciable extent at the ordinary temperature, and naphthalene and ammonia can be recognised by their odour in any specimen of a naphthylhydrazine which has been kept for a long time.

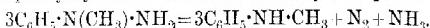
#### *Action of Heat on $\alpha$ -Diphenylhydrazine.*

$\alpha$ -Diphenylhydrazine gave off a little ammonia when melting, but no noticeable evolution of gas occurred until about  $260$ — $270^{\circ}$ , when nitrogen and ammonia were rapidly evolved and so much heat liberated that action continued after the withdrawal of the flame. After heating some time to  $287$ — $288^{\circ}$ , evolution of gas ceased, and the residue proved, on distillation, to be practically pure diphenylamine, only a little black tar being left behind in the distilling flask. No diphenyl could be recognised. The action was found to proceed practically quantitatively according to the equation:

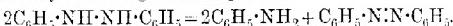


*Action of Heat on *as*-Phenylmethylhydrazine.*

Fifteen grams of *as*-phenylmethylhydrazine were made to boil gently for about eight hours in the apparatus previously described, the air having been displaced as before by hydrogen. Nitrogen and ammonia were continuously evolved. When evolution of gas had ceased, the residue in the flask was distilled, and found to consist of methylaniline. The action is thus similar to that which takes place when *as*-diphenylhydrazine is heated, and may be represented thus:

*Action of Heat on *s*-Diphenylhydrazine.*

It has long been known that the hydrazo-compounds, when heated alone, decompose into azo-derivatives and anilines. This was first noted by Hofmann (*Proc. Roy. Soc.*, 1863, **12**, 577) in the paper in which he described the discovery of hydrazobenzene. When hydrazobenzene is heated to about 200°, auto-reduction begins, with so considerable an evolution of heat that if more than a few grams be taken, the reaction proceeds to completion, even if the flame is withdrawn. The product then distils between 210° and 225°, the bulb of the thermometer being immersed in the liquid. The distillate is a red oil, from which azobenzene crystallises on cooling. It consists solely of aniline and azobenzene, the reaction proceeding quantitatively according to the equation :



The *s*-ditolylhydrazines behave exactly similarly on heating, whilst monoacetylhydrazobenzene yields aniline, acetanilide, and azobenzene. The reaction therefore is a general one.

UNIVERSITY CHEMICAL LABORATORY,  
OXFORD.

**LII.—A Synthesis of Derivatives of Phenothioxin.**

By THOMAS PERCY HILDITCH and SAMUEL SMILES.

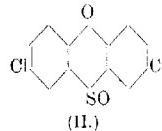
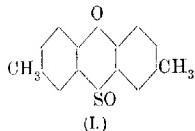
DURING the investigation of certain aromatic hydroxysulphoxides (Gazdar and Smiles, *Trans.*, 1910, **97**, 2248), attempts were made to obtain triarylsulphonium bases from them by condensation with a phenolic ether in presence of concentrated sulphuric acid, but the desired result was not obtained. The negative results obtained with these sulphoxides of *p*-cresol and *p*-chlorophenol seemed

remarkable, for the corresponding ethers, *p*-cresetole and *p*-chlorophenetoles sulphoxides, condense readily under the stated conditions, giving good yields of the aromatic sulphonium salt (compare Smiles and Le Rossignol, Trans., 1908, **93**, 709).

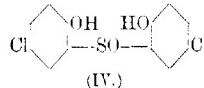
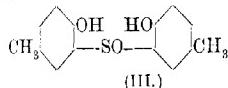
The experiments described in this paper were undertaken with the object of ascertaining the cause of the inactivity of these hydroxy-sulphoxides.

The preparation of the latter substances and their chief derivatives has been described in the previous paper (Gazdar and Smiles, *loc. cit.*). In that place, attention was drawn to the fact that all the hydroxy- or alkylxy-sulphoxides hitherto prepared furnish intensely coloured solutions with concentrated sulphuric acid, and that it is probably the nature of the substances then formed which determines the reactivity of the sulphoxides in this solvent.

It has now been found that the moderately prolonged action of sulphuric acid on the sulphoxides of *p*-cresol and *p*-chlorophenol yields the phenothixin oxides represented by the following formulae:



Taking first the dimethyl compound, it is evident that the sulphoxide from which it is prepared has the structure (III),



for the dimethyl ether obtained from it by methylation is identical with the di-*p*-cresol methyl ether sulphoxide which has been previously shown to have this structure (Le Rossignol and Smiles, Trans., *loc. cit.*). The constitution which is now ascribed to the product obtained from this sulphoxide by the interaction with sulphuric acid is shown by the facts:

1. It is produced by loss of the elements of water from the hydroxy-sulphoxide.
2. When reduced, it loses one atomic proportion of oxygen, and
3. When oxidised, it absorbs the same quantity of that element.
4. Neither the substance itself, nor the products of its oxidation or reduction, contain hydroxyl.

It may also be observed that the molecular weight of the reduction product corresponds with this structure.

From this constitution of the substance, those of the reduction and oxidation products follow; these are respectively the phenothioxin itself (V) and the phenothioxin dioxide (VI):



The constitution of the dichloro-compound cannot be said to be based on such rigid proof as that of the dimethyl derivative, for the structure of the *p*-chlorophenol sulphoxide has not been so definitely established. But the product obtained by the action of sulphuric acid with this sulphoxide so closely resembles dimethylphenothioxin oxide in its chemical character, for example, behaviour on oxidation and reduction, with sulphuric acid, and absence of hydroxyl, that no reasonable doubt can be entertained of the cyclic structure (IV) now assigned to it. It follows thence that the sulphoxide has the constitution indicated above (IV).

Further to confirm the phenothioxin structure for these substances, we have examined the naphthathioxin previously obtained by Mauthner (*Ber.*, 1906, **39**, 1345) from the interaction of  $\beta$ -naphthol sulphide and phosphoryl chloride. This substance may be converted into the oxide by interaction with hydrogen dioxide and into the dioxido with permanganate in glacial acetic acid. The behaviour of these substances agrees closely with that of the derivatives under consideration. Experiments have also been made to obtain the phenothioxins directly from the sulphides of *p*-cresol and of *p*-chlorophenol (compare Gazdar and Smiles, *loc. cit.*) by dehydrating agents. It is remarkable that negative results\* were obtained even with hot sulphuric acid, zinc chloride at 200°, or boiling phosphoryl chloride. Since dichloro- and dimethyl-phenothioxin oxides are formed by the action of cold sulphuric acid on the sulphoxide, it appears that this reaction cannot be one of simple dehydration, for, if it were, it is to be expected that the sulphides would behave similarly, at any rate with hot dehydrating agents.

Such considerations lead to the assumption that the thionyl group plays some part in this reaction, and that the phenothioxine oxides are not the first products. This view is justified by the fact that the maximum yields of the cyclic compounds are only obtained by prolonging the reaction. In fact, if the action be stopped at an early period, by mixing the acid solution with water,

It may be observed that the sulphide of  $\beta$ -naphthol yields the phenoxine with the last named of these reagents (Mauthner, *loc. cit.*), but the behaviour of this sulphide profoundly differs from that of other aromatic ortho-dihydroxysulphides in other respects, for example, oxidation.

entirely different products are obtained. It is thus evident that, although the phenothioxin oxides do not condense with phenolic ethers to give sulphonium salts, the cause of the inactivity of the parent sulphoxides must be sought in these initial products. The nature of the latter is now under investigation.

It may be observed that the phenothioxin oxides are not the only products of the prolonged action of sulphuric acid with the sulphoxides, for the yields are not good, and sulphonation is extensive.

The phenothioxin series is but little known; indeed, previous knowledge of this group is entirely due to Mauthner (*Ber.*, 1905, **38**, 1411; 1906, **39**, 1340), who synthesised two members of the series from *o*-thiophenol and picryl chloride or 4-chloro-3:5-dinitrobenzoic acid. From the last-named substance, the parent compound was obtained by eliminating the nitro- and carboxyl groups.

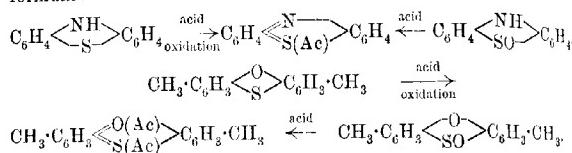
Observations made with the three series of derivatives embraced by the present experiments show that in certain respects these substances resemble the analogous series of thiadiphenylamine. It has been elsewhere shown that the *o*-sulphoxides of diphenylamine yield (Barnett and Smiles, *Trans.*, 1909, **95**, 1253) the intensely coloured azothionium salts with mineral acids, and a similar behaviour has now been observed with the *o*-sulphoxides of diphenyl ether, but in the latter case anhydrous acids of dehydrating power, for example, sulphuric acid, are necessary. Moreover, there is a striking similarity in the action of sulphuric acid on the sulphides of the two series. Thiadiphenylamine is at once oxidised by the cold reagent to the azothionium salt, sulphurous acid being liberated; the phenothioxins are also oxidised by this reagent, giving solutions of an intense blue colour. It may be further observed that these *o*-sulphoxides of diphenyl ether do not contain substituents of strongly acidic character, and they do not yield Naryl derivatives when treated with a phenolic ether in sulphuric acid solution. The same fact has been observed with similar derivatives of diphenylamine *o*-sulphoxide, and it has been shown (Barnett and Smiles, *Trans.*, 1910, **97**, 369) that the disappearance of this characteristic reaction of the thionyl group is due to the immediate conversion of the sulphoxide to the azothionium salt. With sulphoxides of weaker basic power, the rearrangement to azothionium salt proceeds slowly, and the condensation may be effected before this has taken place.

To account for the absence of this characteristic reaction of the thionyl group from the phenothioxin oxides in this solvent, and to display the close analogy between this series and that of thiadiphenylamine, we consider it necessary to represent the products

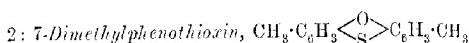
of interaction of the phenothioxin oxides and sulphuric acid as phenothioxonium salts.

Attempts to isolate these substances have not as yet been successful, for on diluting the acid solution they are hydrolysed, and other substances are formed.

The relations between these series are indicated by the following formulæ:



#### EXPERIMENTAL.



*p*-Cresol *o*-sulphoxide, in quantities of 20 grams at a time, was triturated with cold concentrated sulphuric acid, and the solution thus obtained was set aside at the atmospheric temperature for four hours. It was then carefully poured into cold water, and the muddy precipitate was collected and washed with water until free from sulphuric acid. The solid was triturated with aqueous alkali hydroxide, and a little alcohol was added to the mixture, which was then set aside for sixteen hours. The insoluble portion was then collected, washed until free from alkali, dried, and finally crystallised from dilute alcohol. The product melted indefinitely in the neighbourhood of  $65^\circ$ , and analysis showed that it was a mixture of the phenothioxin and its oxide. To obtain the substance in a pure condition, the product was converted into the oxide, and this was reduced.

Dimethylphenothioxin oxide was reduced in hot glacial acetic acid with zinc dust, and when reduction was complete, the excess of zinc dust was removed, and the filtrate mixed with water. An oil was precipitated, which quickly solidified; it was crystallised from dilute methyl alcohol, from which 2: 7-dimethylphenothioxin separated in colourless leaflets, melting at  $74^\circ$ :

0.1926 gave 0.3224 CO<sub>2</sub> and 0.0930 H<sub>2</sub>O. C = 73.9; H = 5.3.  
0.4110, in 16.79 c.c. of benzene gave  $\Delta = -0.547^\circ$ . M.W. = 223.  
C<sub>14</sub>H<sub>12</sub>OS requires C = 73.7; H = 5.2 per cent. M.W. = 228.

Nitric acid readily attacks the substance, but no definite nitro-derivative could be isolated, for, on modifying the conditions, either the interaction was too violent or none took place.

The substance possesses an odour resembling that of geraniums; it is insoluble in water, and readily soluble in most organic media. It dissolves in concentrated sulphuric acid, the solution rapidly becoming blue, whilst sulphurous acid is evolved.

*2: 7-Dimethylphenothioxin Oxide.*

The crude product, obtained as described in a previous paragraph from *p*-cresol *o*-sulphoxide and sulphuric acid, was dissolved in cold glacial acetic acid. To this solution an amount of hydrogen dioxide was added slightly in excess of that required to convert all phenothioxin to its oxide. The mixture was set aside at the atmospheric temperature, and after twenty-four hours it was mixed with water. The solid product was recrystallised from dilute alcohol.

*2: 7-Dimethylphenothioxin oxide* forms colourless needles, which melt at 132–133°. It dissolves in sulphuric acid, the solution being of an intense blue colour:

0·1143 gave 0·2875 CO<sub>2</sub> and 0·0557 H<sub>2</sub>O. C=68·7; H=5·4.  
C<sub>14</sub>H<sub>12</sub>O<sub>2</sub>S requires C=68·8; H=4·9 per cent.

*2: 7-Dimethylphenothioxin Dioxide.*

A solution of the oxide in cold acetic acid was mixed with the calculated quantity of finely powdered potassium permanganate. Solution of the permanganate was assisted by continual shaking, and finally the mixture was set aside for a few hours. Water was then added, and sulphurous acid was passed into the turbid mixture to effect complete decolorisation.

The solid was collected and crystallised from alcohol, when *2: 7-dimethylphenothioxin dioxide* was obtained in colourless prisms, which melted at 172°:

0·1132 gave 0·2693 CO<sub>2</sub> and 0·0485 H<sub>2</sub>O. C=64·88; H=4·8.  
C<sub>14</sub>H<sub>12</sub>O<sub>3</sub>S requires C=64·63; H=4·6 per cent.

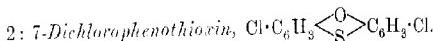
*2: 7-Dichlorophenothioxin Oxide.*

*p*-Chlorophenol *o*-sulphoxide was treated with sulphuric acid in the manner already described with the cresol derivative. Comparative experiments showed that the maximum yields of the phenothioxin derivative (about 25 per cent.) were obtained when the interaction was allowed to proceed for four hours. In this case, however, the product did not appear to contain the phenothioxin, for after it had been recrystallised from alcohol, *2: 7-dichlorophenothioxin oxide* was obtained in shining prisms, which melted at 168°:

0·1005 gave 0·1880 CO<sub>2</sub> and 0·0200 H<sub>2</sub>O. C=51·0; H=2·2.  
 0·1093 „ 0·2035 CO<sub>2</sub> „ 0·0255 H<sub>2</sub>O. C=50·7; H=2·5.  
 $C_{12}H_6O_2Cl_2S$  requires C=50·5; H=2·1 per cent.

The substance gives an intense blue solution with cold sulphuric acid, but no sulphonium base is formed on adding a phenolic ether to this. In one experiment, excess of phenetole was added to the cold solution in sulphuric acid, and after about half an hour had elapsed, this was poured into water. The recrystallised product was found to contain dichlorophenothioxin, and a sample was isolated which melted at 134°. (Found, C=53·2; H=2·7. Calc., C=53·5; H=2·2 per cent.) No sulphonium base could be detected.

Attempts were made to obtain these phenothioxin derivatives by the action of other dehydrating agents with the hydroxy-sulphoxide or sulphide, but with negative results. The reagents employed were fused zinc chloride at 120° and 200°, boiling thionyl chloride, boiling phosphoryl chloride alone or in xylene solution, and boiling phosphorus trichloride. With the latter reagent, the sulphoxide was reduced to sulphide (m. p. 174°). (Found, C=50·3; H=3·1. Calc., C=50·2; H=2·8 per cent.) Warm sulphuric acid acting for one hour also gave negative results with *p*-cresol *o*-sulphide.



This substance was obtained by reducing the phenothioxin oxide with zinc dust in acetic acid, the process being similar to that already described with the dimethyl derivative. It separates from hot alcohol in long, slender needles, which melt at 135°.

0·1163 gave 0·2262 CO<sub>2</sub> and 0·0232 H<sub>2</sub>O. C=53·0; H=2·2.

$C_{12}H_6OCl_2S$  requires C=53·5; H=2·2 per cent.

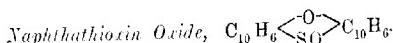
The substance is oxidised by concentrated sulphuric acid.

#### 2:7-Dichlorophenothioxin Dioxide.

This was prepared from the monoxide by oxidation, as described with the dimethyl derivative. It separates from hot alcohol in small, colourless prisms, which melt at 196°:

0·1310 gave 0·2322 CO<sub>2</sub> and 0·0294 H<sub>2</sub>O. C=48·3; H=2·49.

$C_{12}H_6O_3Cl_2S$  requires C=47·8; H=1·99 per cent.



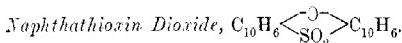
(a) *From Naphthathioxin and Hydrogen Dioxide.*—Naphtha-

thioxin was prepared from  $\beta$ -dihydroxy- $\alpha$ -dinaphthyl sulphide by

interaction with phosphoryl chloride in boiling xylene, as described by Mauthner (*Ber.*, 1906, **39**, 1346). A solution of this substance in a mixture of acetic acid and anhydride, which contained a slight excess of hydrogen dioxide, was set aside at the atmospheric temperature. After four days the mixture was poured into water, and the solid product which then separated was collected and recrystallised from hot acetic acid. Naphthathioxin oxide, prepared in this manner, forms pale yellow needles, which darken and melt at 221°. (Found, C=75·3; H=4·0. Calc., C=75·9; H=3·8 per cent.)

The solutions in sulphuric acid are of a deep blue colour. This substance has been previously prepared by Mauthner (*loc. cit.*) by the oxidation of naphthathioxin with chromic acid. The product of this method was red, but it melted at the same temperature as that now given.

(b) From *β-Dihydroxy-α-dinaphthyl Sulphide and Sulphuric Acid.*—This substance readily dissolves in sulphuric acid, but oxidation sets in immediately, the solution becoming blue, and sulphurous acid being evolved. In one experiment, the mixture was set aside for twenty-four hours, and then dealt with as described in the preparation of the phenothioxin oxides from the sulphoxides of *p*-cresol and *p*-chlorophenol. The product was repeatedly crystallised from hot acetic acid, and finally naphthathioxin oxide was obtained. It was identified by the melting point of a mixture with that substance obtained from other sources.



Naphthathioxin was oxidised in acetic acid solution with potassium permanganate in the usual manner. The product was crystallised from boiling acetic acid, in which it is sparingly soluble. It forms colourless prisms, which melt at 268°.

0·1043 gave 0·2744 CO<sub>2</sub> and 0·0361 H<sub>2</sub>O. C=71·74; H=3·8.  
 $\text{C}_{20}\text{H}_{12}\text{O}_3\text{S}$  requires C=72·3; H=3·6 per cent.

#### *The Ethers of *p*-Cresol and *p*-Chlorophenol α-Sulphorides.*

The methyl ether of *p*-cresol α-sulphoxide was prepared from the corresponding phenol by interaction with methyl iodide in alkaline solution of methyl alcohol. The product of the reaction was treated in a manner similar to that described in the alkylation of phenol α-sulphoxide (*Trans.*, 1907, **91**, 1120). It was purified by crystallisation from ethyl acetate, when it was obtained in colourless prisms, which melted at 134°. A mixture of this substance and the product obtained by direct sulphonation of *p*-tolyl methyl

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ether melted at the same temperature. The constitution of the latter has been previously discussed (Le Rossignol and Smiles, Trans., 1908, 93, 745).

The ethyl ether of *p*-chlorophenol *o*-sulphoxide was prepared by direct sulphination of *p*-chlorophenetole, the process being similar to that formerly described (Le Rossignol and Smiles, *loc. cit.*) with *p*-tolyl methyl ether.

The substance crystallises from ethyl acetate in fine needles, which melt at 145°:

0·1130 gave 0·2234 CO<sub>2</sub> and 0·0485 H<sub>2</sub>O. C=53·9; H=4·7.

C<sub>16</sub>H<sub>16</sub>O<sub>3</sub>Cl<sub>2</sub>S requires C=53·48; H=4·46 per cent.

Both of these ethers of *p*-cresol and *p*-chlorophenol sulphoxide give blue solutions with sulphuric acid, and condense in that medium with phenetole, when the colour is discharged. The corresponding hydroxy-sulphoxides\* do not undergo this condensation under like conditions.

In conclusion, we desire to thank the Research Fund Committee of the Society for a grant which has defrayed the cost of these experiments.

THE ORGANIC CHEMISTRY LABORATORY,  
UNIVERSITY COLLEGE, LONDON.

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LII.— *$\alpha$ -p-Hydroxy-m-methoxyphenylethylamine and the Resolution of  $\alpha$ -p-Hydroxyphenylethylamine.*

By CHARLES WATSON MOORE.

It has several times recently been shown that the enantiomorphously related compounds may differ considerably in their physiological action. Thus, Cushny (*J. Physiol.*, 1904, 30, 176) has shown that *l*-hyosciamine is considerably more active physiologically than the corresponding *d*-base (compare also Trans., 1909, 95, 1969). Similarly, the same author has noted (*Pharm. Journ.*, 1909, 82, 56) that the stereoisomeric epinephrines ("adrenalines") ( $\beta$ -3·4-trihydroxy  $\beta$ -phenylcetyl methylamines) show great differences in the relative intensities of their effect on the blood pressure.

The base  $\alpha$ -*p*-hydroxyphenylethylamine, described by Tutin, Caton, and Hann (Trans., 1909, 95, 2113), exerts an action on the

\* It was formerly stated in error (Gazdar and Smiles, Trans., 1910, 93, 255) that the sulphoxide of *p*-chlorophenol undergoes this condensation.

blood pressure somewhat similar to that of epinephrine, although in a less degree, and, since the former base contains an asymmetric carbon atom, it was considered of interest to ascertain whether the optically active bases, obtained by its resolution, would differ in physiological activity.  $\alpha$ -p-Hydroxyphenylethylamine *d*-camphorsulphonate was therefore prepared and submitted to fractional crystallisation, when the salt of the levorotatory base was easily obtained in a pure condition.

*l*- $\alpha$ -p-Hydroxyphenylethylamine *d*-camphorsulphonate melts at 203–205°, and the specific rotation of the base contained in it, calculated from that of the salt, is  $[\alpha]_D -7.9^\circ$ . The salt of the *d*-base could not be obtained in a pure condition, the specific rotation of the base contained in it being  $[\alpha]_D +6.9^\circ$ . Optically pure benzoyl derivatives were, however, obtained from both of the stereoisomeric bases. The effect on the blood pressure of the *l*- and *d*-bases was determined by Dr. H. H. Dale, of the Wellcome Physiological Research Laboratories, to whom the author now expresses his thanks. No difference in physiological activity between the two bases was observed, and it is therefore evident that in this case the enantiomorphous forms possess an equal degree of physiological activity.

A quantity of acetovanillone (4-hydroxy-3-methoxyacetophenone) being available, it was considered of interest to prepare the corresponding  $\alpha$ -p-hydroxy-m-methoxyphenylethylamine from it. This compound was obtained by the reduction of acetovanilloneoxime, and its hydrochloride and benzoyl derivatives have also been characterised. It has been found by Dr. H. H. Dale, as was anticipated, that the hydroxymethoxy-base is slightly less active physiologically than the above-mentioned  $\alpha$ -p-hydroxyphenylethylamine.

#### EXPERIMENTAL.

##### $\alpha$ -p-Hydroxy-m-methoxyphenylethylamine.

Acetovanillone (4-hydroxy-3-methoxyacetophenone), as obtained from the rhizome of *Apocynum androsaemifolium*, Linné (Moore, Trans., 1909, 95, 734), was converted into its oxime in the usual manner.

Eighteen grams of acetovanilloneoxime were dissolved in 250 c.c. of aqueous methyl alcohol, and twice the theoretical amount of 3 per cent. sodium amalgam gradually introduced, the mixture being kept acid by the frequent addition of acetic acid. When all reaction had ceased, water was added, the alcohol distilled off, and the aqueous liquid extracted with ether to remove unchanged oxime, after which it was rendered alkaline by means of sodium carbonate, and thoroughly extracted with amyl alcohol. The amyl-

alcoholic liquids were extracted with successive quantities of dilute hydrochloric acid, and the combined acid liquids concentrated under diminished pressure, when, on cooling, *α*-p-hydroxy-m-methoxyphenylethylamine hydrochloride separated in glistening prisms. This salt is readily soluble in water and alcohol, but can be recrystallised from a mixture of alcohol and ethyl acetate. The quantity so obtained amounted to about 8·5 grams:

0·1490 gave 0·2938 CO<sub>2</sub> and 0·0936 H<sub>2</sub>O. C=53·7; H=7·0.

0·1710 „ 0·1180 AgCl. Cl=17·0.

C<sub>9</sub>H<sub>13</sub>O<sub>2</sub>N.HCl requires C=53·1; H=6·9; Cl=17·4 per cent.

A methoxyl determination by Perkin's modification of the Zeisel method gave the following result:

0·2136 gave 0·2445 AgI. OMe=15·1.

C<sub>8</sub>H<sub>11</sub>ONCl·OMe requires OMe=15·2 per cent.

*α*-p-Hydroxy-m-methoxyphenylethylamine was obtained from its hydrochloride by the action of sodium ethoxide on an alcoholic solution of the salt. Five grams of the hydrochloride were dissolved in about 25 c.c. of warm absolute alcohol, and to the solution 0·53 gram of sodium, dissolved in 10 c.c. of absolute alcohol, was added. The precipitated sodium chloride was removed by filtration, and the filtrate cooled, when the base separated in glistening prisms, melting at 15°. The quantity so obtained was only 1·5 grams, and on concentrating the alcoholic mother liquor, only amorphous products were obtained. As only 95 per cent. of the theoretical amount of sodium ethoxide was employed for the liberation of the base, this change can only be attributed to the unstable nature of the substance in solution. A similar phenomenon was observed on recrystallising the base, but the latter, when in the crystalline state, is quite stable:

0·1338 gave 0·3180 CO<sub>2</sub> and 0·0970 H<sub>2</sub>O. C=64·8; H=8·0.

0·2806 „ 20·6 c.c. N<sub>2</sub> at 23° and 755 mm. N=8·2.

C<sub>9</sub>H<sub>13</sub>O<sub>2</sub>N requires C=64·7; H=7·8; N=8·4 per cent.

A methoxyl determination by Perkin's modification of the Zeisel method gave the following result:

0·2240 gave 0·3095 AgI. OMe=18·2.

C<sub>8</sub>H<sub>11</sub>ON·OMe requires OMe=18·5 per cent.

The dibenzoyl derivative, prepared by the Schotten-Baumann method, crystallises from alcohol in glistening plates, melting at 178°:

0·1326 gave 0·3574 CO<sub>2</sub> and 0·0686 H<sub>2</sub>O. C=73·5; H=5·7.

C<sub>23</sub>H<sub>21</sub>O<sub>4</sub>N requires C=73·6; H=5·6 per cent.

*α*-p-Hydroxy-m-methoxy-N-benzoylphenylethylamine was obtained by heating the dibenzoyl derivative for some hours with a 10 per

cent. alcoholic solution of potassium hydroxide. It crystallises from alcohol in glistening needles, melting at 168°:

0·1230 gave 0·3170 CO<sub>2</sub> and 0·0711 H<sub>2</sub>O. C=70·3; H=6·4.  
 $C_{18}H_{17}O_3N$  requires C=70·1; H=6·3 per cent.

*The Resolution of  $\alpha$ -p-Hydroxyphenylethylamine.*

$\alpha$ -p-Hydroxyphenylethylamine hydrochloride was first prepared by Tutin, Caton, and Hann (*loc. cit.*), by the reduction of *p*-hydroxyacetophenoneoxime, according to the above-described method for the preparation of  $\alpha$ -p-hydroxy-m-methoxyphenylethylamine hydrochloride. The yield of hydrochloride obtained by these authors was only about 30 per cent. of the theoretical. In view of the above recorded observation respecting the instability of  $\alpha$ -p-hydroxy-m-methoxyphenylethylamine, it seemed advisable to isolate  $\alpha$ -p-hydroxyphenylethylamine hydrochloride without ever liberating the free base. The following modification of the original method was accordingly employed.

Twenty-seven grams of *p*-hydroxyacetophenoneoxime were dissolved in 300 c.c. of aqueous methyl alcohol, and twice the theoretical amount of 3 per cent. sodium amalgam gradually introduced, the mixture being kept acid by the frequent addition of acetic acid. When the reduction was finished, hydrochloric acid, in slight excess, was added, and the solution evaporated to complete dryness under diminished pressure. During the concentration most of the sodium chloride separated, and was removed by filtration. The final residue consisted of the hydrochloride of the base, together with a little sodium chloride, from which the former was obtained by extraction with cold absolute alcohol. The yield was about 70 per cent. of the theoretical.

$\alpha$ -p-Hydroxyphenylethylamine d-camphorsulphonate was obtained by the interaction of  $\alpha$ -p-hydroxyphenylethylamine hydrochloride and silver d-camphorsulphonate in aqueous solution. The precipitated silver chloride was removed by filtration, and the filtrate evaporated to dryness under diminished pressure.

1 $\alpha$ -p-Hydroxyphenylethylamine d-Camphorsulphonate.—The crystalline camphorsulphonate thus obtained was dissolved in hot absolute alcohol, when, on keeping for a short time, a crop of crystals was obtained, melting at 200–202°. On recrystallisation from alcohol, the melting point rose to 203–205°, when it remained constant. The salt forms small, glistening plates, readily soluble in water and hot alcohol:

0·3154 gave 0·2010 BaSO<sub>4</sub>. S=8·7.

$C_{18}H_{27}O_5NS$  requires S=8·7 per cent.

0·4838, made up to 20 c.c. with water, gave, in a 2-dcm. tube,  $\alpha_D + 0^\circ 32'$ , whence  $[\alpha]_D + 11^\circ 0$ ;  $[M]_D + 40^\circ 6$ .

0·4480, made up to 20 c.c. with water, gave, in a 2-dcm. tube,  $\alpha_D + 0^\circ 29'$ , whence  $[\alpha]_D + 10^\circ 8$ ;  $[M]_D + 39^\circ 8$ .

The molecular rotation of *d*-camphorsulphonic acid is  $[M]_D + 51$ ; whence the basic ion has  $[\alpha]_D - 7^\circ 9$ .

The 1-dibenzoyl derivative, prepared by the Schotten-Baumann method, crystallises from alcohol in long needles, melting at 210°;

0·1452 gave 0·4090 CO<sub>2</sub> and 0·0745 H<sub>2</sub>O. C=76·8; H=5·7.  
C<sub>22</sub>H<sub>15</sub>O<sub>3</sub>N requires C=76·5; H=5·5 per cent.

A determination of its specific rotatory power gave the following result:

0·3502, made up to 20 c.c. with chloroform, gave  $\alpha_D - 0^\circ 40'$  in a 2-dcm. tube, whence  $[\alpha]_D - 19^\circ 0$ .

1-*α*-p-Hydroxy-N-benzoylphenylethylamine was formed on heating the dibenzoyl derivative with a 10 per cent. alcoholic solution of potassium hydroxide. It crystallised from dilute methyl alcohol in small, glistening needles, containing 1·5 molecules of water of crystallisation. The anhydrous substance melts at 144°. This substance appears to be dimorphous, as the racemic modification, prepared by Tutin, Caton, and Hann (*loc. cit.*), forms large, hexagonal prisms, melting at 156°:

0·5040 (air dried) gave, on heating at 110°, 0·0495 H<sub>2</sub>O. H<sub>2</sub>O=9·8.  
0·1388\* gave 0·3804 CO<sub>2</sub> and 0·0794 H<sub>2</sub>O. C=74·7; H=6·3.

C<sub>15</sub>H<sub>15</sub>O<sub>2</sub>N, 1·5H<sub>2</sub>O requires H<sub>2</sub>O=10·0 per cent.

C<sub>15</sub>H<sub>15</sub>O<sub>2</sub>N requires C=74·8; H=6·2 per cent.

A determination of its specific rotatory power gave the following result:

0·2150,\* made up to 20 c.c. with chloroform, gave  $\alpha_D - 1^\circ 8$  in a 2-dcm. tube, whence  $[\alpha]_D - 52^\circ 7$ .

The alcoholic mother liquor from which the first crop of crystals had been removed, as above described, was concentrated to a small volume, when a quantity of crystals, melting from 180° to 190°, was obtained. This was removed, and the mother liquor mixed with a large volume of ethyl acetate, when it yielded a final fraction, melting at 163—165°. This final fraction consisted largely of the salt of the dextrorotatory modification, but all attempts to obtain it pure were unsuccessful.

A determination of its specific rotatory power gave the following result:

\* Anhydrous substance.

0·4338, made up to 20 c.c. with water, gave  $\alpha_D + 0^{\circ}42\cdot7'$  in a 1-dcm. tube, whence  $[\alpha]_D + 16\cdot4^\circ$ ;  $[M]_D + 60\cdot5^\circ$ .

The molecular rotation of *d*-camphorsulphonic acid is  $[M]_D + 51^\circ$ , whence the basic ion has  $[\alpha]_D + 6\cdot9^\circ$ .

The *d*-*dibenzoyl* derivative, prepared by the Schotten-Baumann method, crystallised from alcohol in long needles, melting at  $205^\circ$ . After recrystallising from ethyl acetate, the melting point was constant at  $210^\circ$ :

0·1460 gave 0·4104 CO<sub>2</sub> and 0·0745 H<sub>2</sub>O. C = 76·6; H = 5·6.  
 $C_{22}H_{19}O_3N$  requires C = 76·5; H = 5·5 per cent.

A determination of its specific rotatory power gave the following result:

0·3348, made up to 20 c.c. with chloroform, gave  $\alpha_D + 0^{\circ}37'$  in a 1-dcm. tube, whence  $[\alpha]_D + 18\cdot4^\circ$ .

*d*-*a*-*p*-Hydroxy-*N*-benzoylphenylethylamine was formed on heating the dibenzoyl derivative with a 10 per cent. solution of alcoholic potassium hydroxide. It crystallises from dilute methyl alcohol in thinning needles, containing 1·5 molecules of water of crystallisation. The anhydrous substance melts at  $144^\circ$ :

0·2850 (air dried), on heating at  $110^\circ$ , lost 0·0275 H<sub>2</sub>O. H<sub>2</sub>O = 9·6.  
 0·1410 \* gave 0·3880 CO<sub>2</sub> and 0·0796 H<sub>2</sub>O. C = 75·0; H = 6·2.  
 $C_{15}H_{15}O_2N, 1\cdot5H_2O$  requires H<sub>2</sub>O = 10·0 per cent.  
 $C_{15}H_{15}O_2N$  requires C = 74·8; H = 6·2 per cent.

A determination of its specific rotatory power gave the following result:

0·1494,\* made up to 20 c.c. with chloroform, gave  $\alpha_D + 0^{\circ}49'$  in a 1-dcm. tube, whence  $[\alpha]_D + 54\cdot6^\circ$ .

In conclusion, the author wishes to express his thanks to Mr. Frank Tutin for suggesting this investigation.

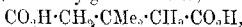
THE WELLCOME CHEMICAL RESEARCH LABORATORIES,  
 LONDON, E.C.

\* Anhydrous substance.

LIII.—*The Formation and Reactions of Imino-compounds. Part XV. The Production of Imino-derivatives of Piperidine Leading to the Formation of the  $\beta\beta$ -Disubstituted Glutaric Acids.*

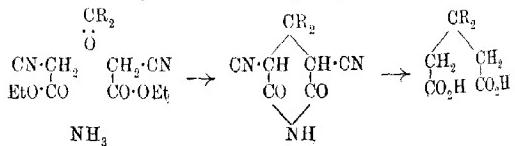
By FERDINAND BERNARD THOLE and JOCELYN FIELD THORPE.

THE methods at present in use for the production of the  $\beta\beta$ -disubstituted glutaric acids are, for the most part, long and tedious operations, requiring the aid of large quantities of expensive material. Thus,  $\beta\beta$ -dimethylglutaric acid,



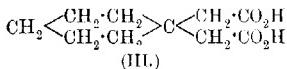
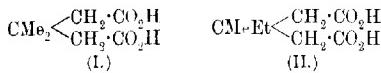
which is the simplest and best known member of this series, can be prepared either by the oxidation of dimethylidihydroresorcinol (Crossley, Trans., 1899, **75**, 777; Komppa, Ber., 1899, **32**, 1423), or by the condensation of ethyl sodiocyanacetate with ethyl  $\beta\beta$ -dimethylacrylate, and the subsequent hydrolysis of the condensation product (Perkin and Thorpe, Trans., 1899, **75**, 49). Both these methods of formation yield the acid in large quantities, but the preparation of the initial material always occupies a considerable period of time; moreover, the above-mentioned reactions have only been applied to the formation of  $\beta\beta$ -dimethylglutaric acid; their application to the formation of higher members of the series would be prohibitive from the point of view of expense of material. Unfortunately, the reactions by which the  $\beta$ -monosubstituted glutaric acids can be prepared, that is, by the condensation of aldehydes with ethyl malonate or ethyl cyanoacetate in the presence of piperidine (Komnenos, Annalen, 1883, **218**, 145; Knoevenagel, Ber., 1898, **31**, 2588), do not yield satisfactory results when the aldehydes are replaced by ketones, and only small yields of the condensation products are obtained by these processes.

This difficulty has been partly overcome by the process introduced by Guareschi (*Atti R. Accad. Sci. Torino*, 1900–1901, **36**, 44%), who condensed ethyl cyanoacetate with ketones in the presence of ammonia, and obtained a piperidine derivative, which yields the  $\beta\beta$ -disubstituted glutaric acid on hydrolysis:



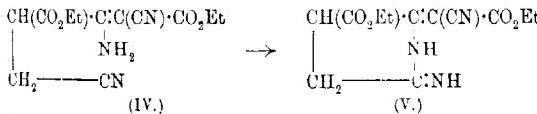
By the aid of this reaction, Guareschi was able to prepare a number of  $\beta\beta$ -disubstituted glutaric acids by varying the nature of the ketone used in the initial condensation.

Although this reaction yields the substituted glutaric acid in a very pure form, we have found it to be a matter of some difficulty to establish the right conditions for the formation of the piperidine derivative in any quantity, and as we wished to prepare a large amount of  $\beta\beta$ -dimethylglutaric acid for the purposes of another research, we decided to search for some method which would yield the acid both rapidly and cheaply. Ultimately we were successful in finding a process, not only leading to the formation of this acid, but one which could be used for the formation of a large number of homologues of glutaric acid substituted in the  $\beta$ -position. As it was thought advisable to establish the general character of this method, three typical examples were selected, namely,  $\beta\beta$ -dimethylglutaric acid (I),  $\beta$ -methyl- $\beta$ -ethylglutaric acid (II), and cyclohexane-1:1-diaceitic acid (III):



and the successive stages of the reaction were carefully followed in each case.

The principle on which the new method is based is as follows. In a previous communication it was shown that an open-chain compound, consisting of four carbon atoms and one nitrogen atom, readily passes into an imino-ring when there is a nitrile group and an amino-group at the opposite ends of the chain. Thus the open-chain compound (IV) was found to pass readily into the pyrrole derivative (V):



The ease with which the piperidine ring is usually formed suggested that in all probability a six-membered open chain of the type (VI) would also pass into the six-membered ring (VII), thus:



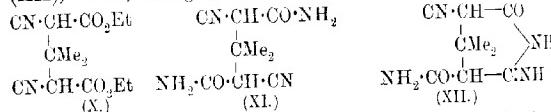
or, in other words, a nitrile-amide of formula (VIII) would pass into an imino-piperidone of formula (IX):



It was, moreover, noticed that imino-compounds of this type are characterised by being practically insoluble in water as well as in most of the usual organic solvents, and it therefore seemed likely that if such a compound could be formed in some simple condensation, it would be at once precipitated from the solution, and hence give rise to a practically quantitative yield of the condensation product, however small the original tendency for its formation might be.

The substance which at once suggested itself as a means of ascertaining this point was cyanoacetamide,  $\text{CN}\cdot\text{CH}_2\text{CO}\cdot\text{NH}_2$ , a compound which has been shown by Henry (*Jahresber.*, 1889, 638) and by Errera (*Gazzetta*, 1896, **26**, 208) to possess properties very similar to those of ethyl cyanoacetate, and to have a hydrogen atom, marked above with an asterisk, which is replaceable by sodium.

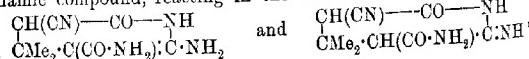
As already mentioned, ethyl cyanoacetate condenses with acetone in the presence of piperidine to give a small yield of the condensation product (X). If therefore cyanoacetamide were substituted for ethyl cyanoacetate, it might be expected that the initial product (XI) would at once pass into the imino-compound (XII), which, owing to its insoluble character, would be pre-



cipitated from the solution, giving rise to a fresh production of condensation product, and this in its turn would be precipitated, and so on until the reaction was complete.

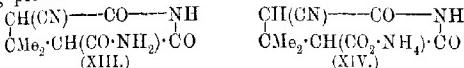
This assumption proved to be correct, for it was found that when two molecular proportions of cyanoacetamide and one of acetone were dissolved in cold water and treated with a small quantity of piperidine or aqueous sodium hydroxide, the resulting yellow solution slowly deposited a crystalline precipitate, which, when complete, weighed more than the amount of cyanoacetamide used in the experiment.

Investigation showed this substance to be a tautomeric ketimino-enamic compound, reacting in the two forms:



but having a very short imino-phase,\* a conclusion which was arrived at as the result of the following experiments:

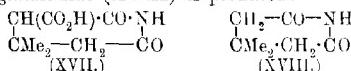
(1) The substance is a mono-acid base, and yields a well-defined platinichloride. It forms a clear solution with dilute hydrochloric acid, which, if immediately treated with sodium acetate, deposits the imino-compound practically unchanged, but, if allowed to remain, slowly deposits the imide (XIII), formed by the hydrolysis of the imino-form of the tautomeric compound. The transformation of the imino-compound (XII) into the imide (XIII) is complete if the solution of the base in dilute hydrochloric acid is raised to the boiling point:



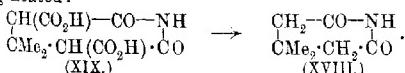
(2) When the base (XII) is boiled for a long time with water, ammonia is eliminated, and if the operation is continued until all ammonia has been evolved, the product is found to be the cyano-acid (XV). It is evident that the ammonium salt of this acid (XIV) is first formed, but that on boiling with water it dissociates, yielding the free acid:



(3) When the above cyano-acid (XV) is heated, carbon dioxide is eliminated, and the nitrile (XVI) is formed. This substance is also produced when a solution of the base (XII) in dilute hydrochloric acid is boiled for some hours. When the cyano-acid is boiled with alkali, the alkali salt of the carboxylic acid (XVII) is formed, and when the free acid is heated, carbon dioxide is evolved, and  $\beta\beta$ -dimethylglutarimide (XVIII) is produced:



(4) When the base (XII) is treated with excess of sodium hydroxide, it forms a clear yellow solution, the colour of which disappears on boiling, ammonia being subsequently evolved on further heating. The ultimate product, after all ammonia has been eliminated, is the alkali salt of the dibasic acid (XIX), the free acid from which passes into  $\beta\beta$ -dimethylglutarimide (XVIII) on being heated:



\* As the compound gives no colour with ferric chloride there is probably no enolic phase.

The yield of  $\beta\beta$ -dimethylglutarimide by this last process is not very good, as the action of alkali on the base also proceeds in another direction, with the formation of some acetone and malonic acid. The cause of this rather remarkable decomposition is still under investigation.

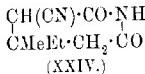
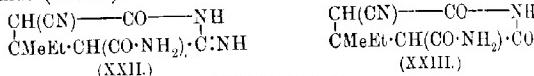
(5) When the base (XII) is heated with 70 per cent. sulphuric acid for three hours, it is quantitatively converted into  $\beta\beta$ -dimethylglutaric acid (XXI):



The constitution of the condensation product of cyanoacetamide and acetone is there clearly established. In order, however, to show that the method is of general application, we decided, as already mentioned, to investigate two other cases, and selected methyl ethyl ketone and cyclohexanone for experiment.

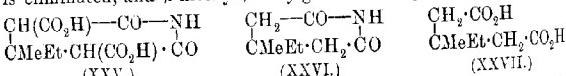
Both these ketones readily condense with cyanoacetamide in the presence of piperidine or sodium hydroxide, and in each case a satisfactory yield of the condensation product is obtained.

Methyl ethyl ketone yields the imino-compound (XXII), which, on warming with dilute hydrochloric acid, is converted into the imide (XXIII):



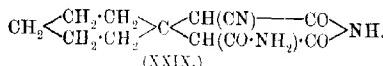
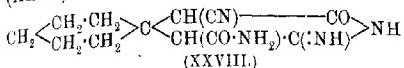
from which the nitrile (XXIV) is produced by the prolonged action of boiling dilute hydrochloric acid.

Alkalies hydrolyse the imino-compound to the dibasic acid (XXV), but here again a certain amount of methyl ethyl ketone is regenerated during the hydrolysis, and the yield of the dibasic acid is, consequently, not good. When the acid is heated, carbon dioxide is eliminated, and  $\beta$ -methyl- $\beta$ -ethylglutarimide (XXVI) is formed:

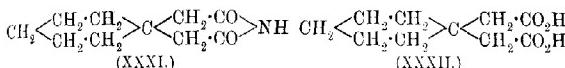
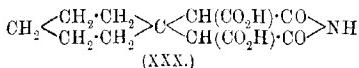


When the imino-compound (XXII) is boiled with 70 per cent. sulphuric acid, it is completely transformed into  $\beta$ -methyl- $\beta$ -ethylglutaric acid (XXVII). This acid has been prepared by Guareschi (*loc. cit.*), but was not characterised by the formation of derivatives. We have therefore prepared the anhydride and the naphthylamic acid.

The imino-compound (XXVIII), which is formed from *cyclo*-hexanone and cyanoacetamide, undergoes a similar series of changes. Thus, with warm dilute hydrochloric acid, it yields the imide (XXIX):



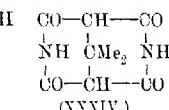
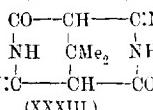
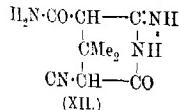
When boiled with aqueous potassium hydroxide until free from ammonia, some cyclohexanone is eliminated, but it is, for the most part, converted into the dibasic acid (XXX), which, on being heated, is converted into the imide of cyclohexane-1:1-diacetic acid (XXXI). With sulphuric acid, the imino-compound (XXXVII) is completely converted into cyclohexane-1:1-diacetic acid (XXXII):



*cyclo*Hexane-1 : 1-diacetic acid is a well-defined crystalline substance, which melts at 181°, and gives an anhydride melting at 73°. It was characterised by the formation of derivatives.

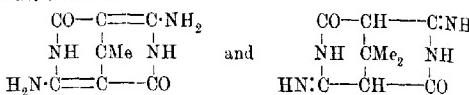
These examples therefore show clearly that the method, so far as the simpler ketones are concerned, is of general application, and that by its means the  $\beta\beta$ -disubstituted glutaric acids can be readily prepared in quantity.

During the experiments with these imino-compounds derived from ketones and cyanoacetamide, it was noticed that under certain conditions they readily undergo a further imino-condensation with the formation of a second six-membered ring having three carbon atoms in common with the first. Thus, when the imino-compound derived from acetone and cyanoacetamide (XII) is treated with sodium ethoxide in alcohol, a sparingly soluble sodium salt is formed, which, when treated in aqueous solution with acetic acid, yields a crystalline substance the reactions of which show it to be the di-iminodi-imide represented by formula (XXXIII):



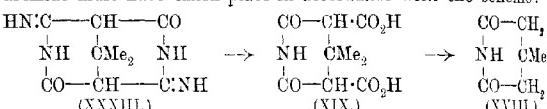
The constitution of this substance follows from the following experimental data:

(1) It is a di-acid, tautomeric di-imino-diamino-compound, reacting in the two forms:



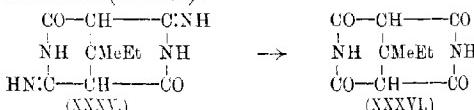
but has only a short imino-phase. This is shown by its behaviour towards dilute hydrochloric acid, in which it forms a clear solution when cold, but from which the original substance is precipitated practically unchanged on the addition of sodium acetate. When the solution in dilute hydrochloric acid is warmed, both imino-groups are at once eliminated, and the di-imide (XXXIV) is precipitated from the hot solution.

(2) When boiled with aqueous potassium hydroxide, one imido-ring is broken, and if the action of the alkali is continued until all ammonia has been evolved, the dibasic acid (XIX) can be obtained from the product. The constitution of this dibasic acid was proved, as in the former case, by the production of  $\beta\beta$ -dimethylglutarimide from it on heating, and therefore the decomposition of the di-imino-di-imide must have taken place in accordance with the scheme:

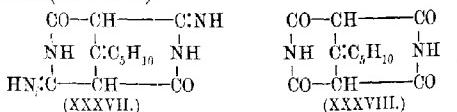


(3) When boiled with 70 per cent. sulphuric acid, the di-imino-di-imide is completely converted into  $\beta\beta$ -dimethylglutaric acid.

The formation of the double ring is also shown by the imino-compounds from methyl ethyl ketone and *cyclohexanone* (XXII and XXVIII). Thus, the first-named yields the di-imino-di-imide (XXXV), which, on warming with dilute hydrochloric acid, passes into the di-imide (XXXVI):



whilst the imino-compound from *cyclohexanone* yields the di-imino-di-imide (XXXVII), which is converted by hydrochloric acid into the di-imide (XXXVIII):

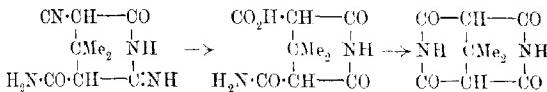


These substances behave in the same manner as the di-imino-di-imide from acetone, and are completely hydrolysed by sulphuric acid to the corresponding  $\beta\beta$ -disubstituted glutaric acids.

The formation of the double ring in this manner is certainly remarkable, but the fact that it is so readily broken by alkali hydroxide, when, as is well known, the imides of the glutaric series are very stable towards this reagent, shows that it is under greater strain than the single ring.

The double ring is, however, produced by other reagents than sodium ethoxide; thus it is the first product formed by the action of aqueous alkali hydroxides on the imino-imides. This fact can be demonstrated in the following way. When the imino-imide is dissolved in dilute aqueous alkali, a yellow solution is formed, the colour of which is rapidly discharged on warming. If the solution is cooled as soon as the colour has disappeared and is then acidified with acetic acid, the di-imino-di-imide is precipitated in the pure condition.

The double-ring compounds are also formed under conditions which usually yield the single-ring imides from the corresponding  $\gamma$ -nitrile carboxylic acids. Thus, when the imino-imides are boiled with dilute sulphuric acid, the clear solution, on being boiled, slowly deposits the crystalline bicyclic di-imide. This reaction is probably represented by the scheme:



and does not involve the previous formation of the di-imino-di-imido-compound.

#### EXPERIMENTAL.

##### Cyanoacetamide, $\text{CN}\cdot\text{CH}_2\cdot\text{CO}\cdot\text{NH}_2$ .

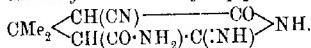
This substance was originally prepared by Hoff (*Jahresber.*, 1874, 561), and more recently by Henry (*Bull. Soc. chim.*, 1887, [ii], **48**, 656) and Illesse (*Amer. Chem. J.*, 1896, **18**, 724). We find that it may be quickly prepared by the following simplified process.

One hundred grams of ethyl cyanoacetate are mixed in a wide-mouthed stoppered bottle with 75 c.c. of strong ammonia, and shaken vigorously. After three minutes the solution becomes homogeneous and warm, when it is cooled under running water and shaken for twenty minutes. The crystals are then collected, washed with a little cold alcohol, and recrystallised from a small amount of hot alcohol. The yield obtained in this way is 85 per cent. of the theoretical, and a further quantity, representing 10 per cent., can be recovered from the mother liquors on evaporating them under

diminished pressure. Pure cyanoacetamide forms colourless needles, which melt at 118·5°.

*Condensation of Acetone with Cyanoacetamide: 6-Imino-3-cyano-*

*5-carbamyl-4:4-dimethyl-2-piperidone,*



This condensation is effected in aqueous solution in the presence of a small quantity of piperidine or alkali hydroxide; the conditions found to give the best yield were as follows.

One hundred grams of cyanoacetamide were dissolved in a sufficient quantity of cold water, and the clear solution was mixed with 45 grams of acetone.\* The solution was then warmed to 20°, and 1 c.c. of piperidine or 1 c.c. of a 30 per cent. solution of potassium hydroxide in water added, the solution being kept for twenty-four hours. At the end of this time the large quantity of crystalline material which had separated was filtered from the yellow solution, washed with water, and dried on a porous plate. It weighed 105 grams (theory, 123 grams), and was found to be completely soluble in cold dilute hydrochloric acid. The mother liquor from the crystals deposited, after some time, a further small quantity of crystalline material, only part of which dissolved in dilute hydrochloric acid. The two substances present in this mixture were separated by grinding with cold dilute hydrochloric acid, filtering, and precipitating the soluble portion from the filtrate by the addition of sodium acetate solution. In this way a further 10 grams of basic substance were obtained identical with that derived from the first precipitation, giving therefore a total yield of 93 per cent. The piperidone derivative obtained in this manner crystallises from water in small, colourless prisms, which melt to a yellow liquid, and then decompose at 234°. The base is only very sparingly soluble in the usual organic solvents, and since recrystallisation from water gives rise to a certain amount of decomposition, it is best purified by dissolving in cold dilute hydrochloric acid and reprecipitating by the addition of sodium acetate:

0·1895 gave 0·3588 CO<sub>2</sub> and 0·1006 H<sub>2</sub>O. C=51·64; H=5·9.

0·1551 „ 37·0 c.c. N<sub>2</sub> at 19° and 733 mm. N=26·95.

C<sub>9</sub>H<sub>12</sub>O<sub>2</sub>N<sub>4</sub> requires C=51·9; H=5·8; N=26·9 per cent.

The piperidone derivative reacts as a monacid base, and forms stable salts with mineral acids.

The *platinichloride* separates as a yellow, sandy powder when a solution of platinic chloride is added to a concentrated solution of

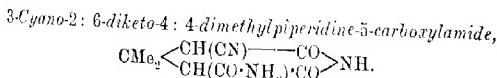
\* In the earlier experiments acetone from the bisulphite compound was used. It was found later that commercially pure acetone gave equally good results.

the base in excess of hydrochloric acid. Care must be taken, however, to keep the temperature as low as possible, and to facilitate the separation of the salt by scratching; otherwise some ammonium platinichloride will also separate, owing to the hydrolysis of the imino-group by the hydrochloric acid present:

0·330 gave 0·0770 Pt. Pt = 23·33.

$(C_9H_{12}O_2N_4)_2H_2PtCl_6$  requires Pt = 23·5 per cent.

When the piperidone base is boiled for a long time with water, ammonia is evolved together with some acetone; the compounds formed are described on p. 432. It dissolves in aqueous sodium hydroxide, forming a yellow solution, from which the colour is discharged on warming; the cause of this change is explained on p. 436. The prolonged action of boiling alkali yields  $\beta\beta$ -dimethyl-glutarimide as chief product, whereas the ultimate hydrolysis by concentrated mineral acids gives a quantitative yield of  $\beta\beta$ -dimethyl-glutaric acid. During the preparation of the above piperidone base either by the aid of piperidine or of alkali hydroxide, a small quantity of a second substance is always produced. In the piperidine experiment, this substance separates from the mother liquor on keeping after the imino-compound has been collected, and can be readily isolated from the chief product of the reaction, owing to its insolubility in dilute hydrochloric acid. In the potassium hydroxide experiment, the same substance separates when the alkaline filtrate is acidified by acetic acid, and is in this case entirely free from the chief product of the reaction. The amount formed under the experimental conditions described is not more than 5 per cent., although the quantity is considerably increased if the temperature during the condensation is kept too high. It crystallises from alcohol in small needles, which melt at 212°, and yield malonic acid on complete alkaline hydrolysis. We have not as yet succeeded in assigning a satisfactory constitution to this substance.



This compound is formed by the action of hot dilute hydrochloric acid on the piperidone base under the following conditions.

Ten grams of the base were suspended in 20 c.c. of water, and a sufficient quantity of hydrochloric acid was added to effect complete solution. The mixture was then raised to the boiling point, and kept at this temperature for one minute, when it was cooled and scratched with a glass rod. Crystals of the imide immediately

separated, which, when recrystallised from hot water, yielded long, colourless needles, melting and evolving gas at 250°:

0·1465 gave 0·2766 CO<sub>2</sub> and 0·0705 H<sub>2</sub>O. C=51·5; H=5·35.

0·2238 „ 39·0 c.c. N<sub>2</sub> at 19° and 743 mm. N=20·01.

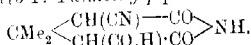
C<sub>9</sub>H<sub>11</sub>O<sub>3</sub>N<sub>3</sub> requires C=51·7; H=5·3; N=20·1 per cent.

The imide dissolves in dilute aqueous sodium carbonate, forming a clear solution, from which a colourless sodium salt separates if the solution is concentrated. It is unchanged on prolonged boiling with water, but, when heated with aqueous sodium hydroxide, evolves ammonia, and is ultimately converted into ββ-dimethyl-glutarimide. The products formed on acid hydrolysis are the same as those produced from the piperidone base.

*The Action of Hydrolysing Agents on 6-Imino-3-cyano-5-carbamyl-4: 4-dimethylpiperidone.*

(a) Water.

3-Cyano-2: 6-diketo-4: 4-dimethylpiperidine-5-carboxylic Acid,



When the imino-compound is boiled for a long time with water, ammonia is evolved, together with some acetone, and at the same time a small quantity of the di-imino-di-imide of ββ-dimethyl-propane-αγγ-tetracarboxylic acid (see p. 435) is precipitated as colourless crystals. If the filtrate from these crystals is then boiled until free from ammonia, the solution, on evaporation, yields a gummy residue, which consists of a mixture of the above acid and its ammonium salt. The residue readily dissolves in water, and the solution, on being acidified by hydrochloric acid, deposits the above acid in colourless crystals. When recrystallised from water, it forms small prisms, which melt and evolve carbon dioxide at 221°:

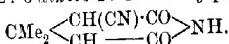
0·1344 gave 0·2518 CO<sub>2</sub> and 0·0591 H<sub>2</sub>O. C=51·21; H=4·91.

0·1474 „ 17·1 c.c. N<sub>2</sub> at 14° and 738 mm. N=13·46.

C<sub>9</sub>H<sub>10</sub>O<sub>4</sub>N<sub>2</sub> requires C=51·4; H=4·8; N=13·3 per cent.

The acid is characterised by giving a sparingly soluble sodium salt and ammonium salt. The former separates when sodium carbonate solution is added to a dilute aqueous solution of the acid.

3-Cyano-2: 6-diketo-4: 4-dimethylpiperidine,



When the nitrile-carboxylic acid described above is heated over its melting point until all carbon dioxide has ceased to be evolved,

an oil remains, which solidifies on cooling. When recrystallised from hot water, it forms long, colourless needles, melting at 200°. Owing to the high temperature required for this decomposition, the yield of the nitrile is not good; consequently it is better to prepare this substance by the action of dilute hydrochloric acid on 6-imino-3-cyano-5-carbamyl-4:4-dimethyl-2-piperidone. For this purpose, the piperidone derivative is dissolved in dilute hydrochloric acid (10 per cent.), and boiled for twelve hours. The product is filtered from a small quantity of the insoluble di-imide of  $\beta\beta$ -dimethylpropane- $\alpha\gamma\gamma$ -tetracarboxylic acid (see p. 436), and the filtrate evaporated to a small bulk. The crystals which separate are identical with those produced from the nitrile-carboxylic acid in the manner described above:

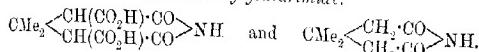
0·1685 gave 0·3548 CO<sub>2</sub> and 0·0917 H<sub>2</sub>O. C=57·41; H=6·10.  
0·1181, 17·9 c.e. N<sub>2</sub> at 14° and 733 mm. N=17·1.

C<sub>8</sub>H<sub>10</sub>O<sub>2</sub>N<sub>2</sub> requires C=57·8; H=6·0; N=16·9 per cent.

The nitrile slowly dissolves in aqueous sodium carbonate solution. Both the nitrile and its carboxylic acid pass into  $\beta\beta$ -dimethylglutarimide when boiled with potassium hydroxide.

(b) Potassium Hydroxide.

*The Imide of  $\beta\beta$ -Dimethylpropane- $\alpha\gamma\gamma$ -tetracarboxylic Acid and  $\beta\beta$ -Dimethylglutarimide.*



When the piperidone base is mixed with rather more than the calculated quantity of potassium hydroxide dissolved in water, a clear yellow solution is formed, from which the colour is discharged on warming, a change which is very clearly defined, and is due to the formation of the alkali salt of the double ring in a manner explained on p. 436. When the colourless solution is boiled, ammonia, together with some acetone, is evolved, and if the heating be continued until all ammonia has been driven off, for which purpose five hours are usually required, the solution will be found to contain the potassium salt of the above acid, together with  $\beta\beta$ -dimethylglutarimide. The acid is best isolated by acidifying the solution with hydrochloric acid and evaporating to dryness with sand and ammonium sulphate, during which process a certain quantity of  $\beta\beta$ -dimethylglutarimide, formed by the elimination of carbon dioxide from the dicarboxylic acid, sublimes on the sides of the vessel in long needles. The residue is then extracted in a Soxhlet apparatus with alcohol, and the alcoholic extract, after being evaporated to dryness, is mixed with ether. The dicarboxylic acid is quite

insoluble in ether, whereas the imide dissolves if a sufficient quantity of the solvent is used. Consequently, by repeatedly rubbing the residue with ether, the acid is ultimately obtained pure. It crystallises from water in small prisms, which melt and evolve carbon dioxide at 225–230°:

0·2001 gave 0·3463 CO<sub>2</sub> and 0·0882 H<sub>2</sub>O. C=47·21; H=4·88.

C<sub>9</sub>H<sub>11</sub>O<sub>6</sub>N requires C=47·3; H=4·8 per cent.

The ethereal extract furnished a solid residue on evaporation; this crystallised from water in long needles, melting at 147°, which proved to be those of  $\beta\beta$ -dimethylglutarimide. The amount of the imide formed in the hydrolysis depends on the length of the time during which the hydrolysis is allowed to proceed, and if the action is continued for a long time scarcely any of the dicarboxylic acid is formed. The imide is produced in quantitative yield when the dicarboxylic acid is distilled under ordinary pressure; its constitution was established by analysis (Found, C=59·43; H=7·8; silver salt Ag=43·82. Calc., C=59·6; H=7·8; silver salt Ag=43·7 per cent.), and its identity with  $\beta\beta$ -dimethylglutarimide was proved by direct comparison with a specimen of this substance prepared from  $\beta\beta$ -dimethylglutaric acid.

(c) *Mineral Acids.*—The action of hot dilute mineral acids, such as hydrochloric acid and sulphuric acid, on the piperidone derivative leads, as already mentioned, to the formation of the corresponding imide. Further action of the hot dilute acid then produces other changes, the reaction proceeding in two directions. One of these causes the ultimate hydrolysis of the compound to  $\alpha$ -cyano- $\beta\beta$ -dimethylglutarimide (see p. 432); the other leads to the precipitation of the very insoluble di-imide of  $\beta\beta$ -dimethylpropane- $\alpha\gamma\gamma$ -tetracarboxylic acid (see p. 436), which is not acted on by boiling with dilute acids. By far the greater quantity of the piperidone derivative follows the second direction, and if, therefore, a solution of the base in dilute sulphuric acid is boiled, the clear solution slowly deposits a crystalline precipitate of the di-imide, which is usually complete after three hours. When the filtrate from this compound is evaporated, it yields  $\alpha$ -cyano- $\beta\beta$ -dimethylglutarimide (see p. 432).

#### $\beta\beta$ -Dimethylglutaric Acid.

As the processes described in this paper originated in a desire to prepare  $\beta\beta$ -dimethylglutaric acid in quantity, it is advisable to describe the method by which we have succeeded in obtaining large amounts of this acid from the piperidone base.

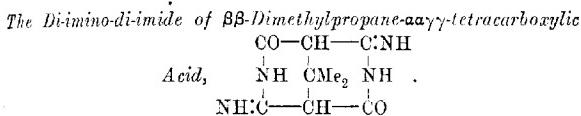
One hundred grams of the base are placed in a litre flask, and mixed with 150 grams of concentrated sulphuric acid. Thirty c.c.

of water are then added to the hot solution, and the liquid heated on the sand-bath until the evolution of carbon dioxide, which is very vigorous, has ceased.

When this occurs, which is usually about one hour after the heating has been started, a further 50 c.c. of water are added, and the solution boiled on the sand-bath for five hours. It sometimes happens that owing to the sulphuric acid not being sufficiently strong, some separation of the insoluble di-imide takes place after the addition of the second quantity of water; this dissolves, however, on further heating.

A considerable quantity of acid separates from the acid solution on cooling, but it is advisable to add some water, saturate the solution with ammonium sulphate, and extract with ether, as a purer product is obtained in this manner than by filtering the strongly acid solution directly.

The acid prepared in this way possesses a high degree of purity, and can be at once used without further purification. The yield from the piperidone base is quantitative. The acid melted at 101°, and was characterised by analysis (Found, C=52·3; H=7·5. Calc., C=52·5; H=7·5 per cent.), and by the formation of its anhydride.



This compound is produced from 6-imino-3-cyano-5-carbamyl-4: 4-dimethyl-2-piperidone by the action of alkali, either in the form of sodium ethoxide or of sodium hydroxide. It is also formed, as already mentioned, as a by-product in the hydrolysis of the piperidone base by acids. The preparation by means of sodium ethoxide may be effected as follows: Ten grams of the finely-ground base are suspended in 75 c.c. of alcohol, and a solution containing 2·3 grams of sodium in 30 c.c. of alcohol is added. The addition of sodium ethoxide causes the base to dissolve, forming a clear yellow solution, from which, on warming on the water-bath, a colourless, crystalline sodium compound separates, and at the same time the yellow colour of the solution disappears. The sodium compound is then collected, washed with a little alcohol, and dried. The specimen analysed was dried at 80°, but the figures showed that it contained one molecule of alcohol of crystallisation:

0·3734 gave 0·1734 Na<sub>2</sub>SO<sub>4</sub>. Na=15·1.

0·3306 " 0·1546 Na<sub>2</sub>SO<sub>4</sub>. Na=15·2.

C<sub>9</sub>H<sub>10</sub>O<sub>2</sub>N<sub>2</sub>Na<sub>2</sub>C<sub>2</sub>H<sub>6</sub>O requires Na=15·4 per cent.

It was not found possible to obtain a satisfactory analysis of the compound free from alcohol, as the temperature required to drive off the solvent caused appreciable decomposition of the salt.

The sodium salt is very deliquescent, and readily takes up moisture from the air. It dissolves in water, forming an alkaline solution, which, when acidified by acetic acid, deposits the base as a heavy, white precipitate, which is insoluble in all the usual solvents, and is best purified by dissolving in cold dilute hydrochloric acid and reprecipitating by the addition of sodium acetate solution. In this way it is obtained in small needles, which sublime at a high temperature without melting:

0·1555 gave 0·2929 CO<sub>2</sub> and 0·0844 H<sub>2</sub>O. C=51·41; H=6·01.

0·1654 „, 38·2 c.c. N<sub>2</sub> at 20° and 750 mm. N=26·66.

C<sub>9</sub>H<sub>12</sub>O<sub>2</sub>N<sub>4</sub> requires C=51·9; H=5·8; N=26·9 per cent.

The di-imino-di-imide can also be formed by the aid of aqueous potassium hydroxide in the following way. Five grams of the piperidone base are dissolved in a sufficient quantity of dilute aqueous potassium hydroxide, and the clear yellow solution is warmed on the water-bath. After a few minutes, it becomes colourless, and if at this stage the solution is quickly cooled and acidified by acetic acid, the dicyclic base is precipitated. The end-point of the reaction is very clearly defined, and can be easily distinguished in daylight.

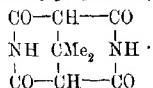
The compound is a di-acid base, and forms salts with two equivalents of hydrochloric acid. It dissolves in aqueous alkali, forming a colourless solution.

The *platinichloride* separates as lustrous, yellow plates when a solution of the base containing excess of hydrochloric acid is mixed with a solution of platinic chloride. The precipitation should be hastened by scratching, and the solution kept as cold as possible:

0·3944 gave 0·1238 Pt. Pt=31·4.

C<sub>9</sub>H<sub>12</sub>O<sub>2</sub>N<sub>4</sub>H<sub>2</sub>PtCl<sub>6</sub> requires Pt=31·5 per cent.

*The Di-imide of ββ-Dimethylpropane-αγγ-tetracarboxylic Acid,*



When a solution of the di-imino-di-imide in dilute hydrochloric acid is warmed, the solution remains clear for a few minutes, and then slowly deposits glistening plates of the above compound. The same substance is also formed in small amount during the acid hydrolysis of the piperidone base in the manner already described.

It is insoluble in all the usual solvents, and sublimes at a high temperature without melting:

0·1384 gave 15·8 c.c. N<sub>2</sub> at 14° and 755 mm. N=13·5.

C<sub>9</sub>H<sub>10</sub>O<sub>4</sub>N<sub>2</sub> requires N=13·3 per cent.

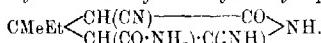
The compound is soluble in aqueous alkalies, and behaves in a characteristic manner when treated in ammoniacal solution with silver nitrate. Thus, when a solution in excess of ammonia is mixed with aqueous silver nitrate, a clear solution is formed, quickly changing to a clear transparent jelly, which slowly becomes opaque on keeping.

*The Products of Hydrolysis of the Dicyclic Compounds described above.*

As mentioned in the introduction, the second ring of the compounds described above is less stable towards hydrolysing agents than that of the single five-membered cyclic imides. Thus, when either the di-imino-di-imide or the di-imide is boiled with excess of aqueous alkali hydroxide, ammonia is evolved, and the ultimate product is  $\beta\beta$ -dimethylglutarimide. No acetone is evolved during this hydrolysis, and the yield of the imide is practically quantitative. The compounds are not affected by aqueous alkali carbonates even on prolonged boiling. With acid hydrolysing agents, the hydrolysis is a matter of some difficulty, owing to the insolubility of the di-imide in all acids excepting concentrated sulphuric acid. Thus prolonged boiling with concentrated hydrochloric acid is without effect, and when the di-imino-di-imide is used, the clear solution, which is first formed, at once deposits the insoluble di-imide on warming. The only way to hydrolyse these compounds by acids is to use concentrated sulphuric acid, and to add only a very little water. The sulphuric acid should not be weaker than 85 per cent., and the clear solution should then be kept at about 150° until the evolution of carbon dioxide has ceased; more water may then be added, and the hydrolysis continued for five hours. In this way a quantitative yield of  $\beta\beta$ -dimethylglutaric acid can be obtained.

*The Condensation of Methyl Ethyl Ketone with Cyanoacetamide:*

*6-Imino-3-cyano-5-carhamyl-4-methyl-4-ethyl-2-piperidone,*



This condensation was effected in much the same manner as described previously in the case of acetone, although, in this instance, the formation of the condensation product does not take place so readily, and the reaction requires a longer time. The conditions found to give the best results were as follows.

One hundred grams of cyanoacetamide were dissolved in a sufficient quantity of water, and mixed with 55 grams of methyl ethyl ketone. The solution was then warmed to 20°, and 1 c.c. of piperidine added. The clear yellow solution slowly deposited the piperidone base in colourless needles, the separation being complete after forty-eight hours, when the product was collected and dried. It was found to weigh 108 grams, and to be completely soluble in cold dilute hydrochloric acid. The filtrate deposited a further small quantity of crystalline material on keeping, which only partly dissolved in dilute hydrochloric acid. The soluble portion was therefore isolated by filtration, and the base precipitated from the solution by the addition of sodium acetate. In this way a further 8 grams were obtained. The base, as in the case of the corresponding acetone compound, is slowly decomposed by boiling water; it was therefore purified for analysis by dissolving in cold dilute hydrochloric acid, and precipitating from the filtered solution by the addition of sodium acetate. It is obtained in this way in lustrous plates, which melt and decompose at 225°:

0·1719 gave 0·3396 CO<sub>2</sub> and 0·0999 H<sub>2</sub>O. C=53·91; H=6·52.

0·1639 „ 36·3 c.c. N<sub>2</sub> at 19° and 730 mm. N=25·0.

$C_{10}H_{14}O_2N_4$  requires C=54·0; H=6·3; N=25·2 per cent.

The compound is a monacid base, and the hydrochloride separates in small needles when concentrated hydrochloric acid is added to a dilute solution of the salt.

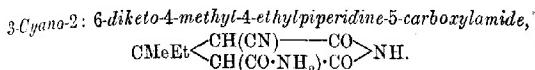
The platinichloride separates in pale yellow plates when a solution of the base in excess of hydrochloric acid is mixed with platinic chloride solution:

0·1812 gave 0·0411 Pt. Pt=22·68.

$(C_{10}H_{14}O_2N_4)_2PtCl_6$  requires Pt=22·7 per cent.

The piperidone base dissolves in aqueous potassium hydroxide, forming a yellow solution from which the colour is discharged on warming, a change which is due to the formation of the potassium salt of the di-imino-di imide. Prolonged boiling with alkali hydroxide yields  $\beta\beta$ -methylmethylethylglutarimide, whilst complete hydrolysis with concentrated sulphuric acid furnishes a quantitative yield of  $\beta\beta$ -methylmethylethylglutaric acid.

The by-product corresponding with the substance melting at 212° formed in the acetone experiment is also produced in the present condensation, although in smaller quantity. It is separated from the piperidone base, as already described, by rubbing with dilute hydrochloric acid, and crystallises from alcohol in large, colourless prisms, which melt at 192°. As the analyses furnished no clue to the constitution of this substance, it was laid aside for further investigation.



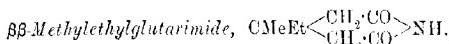
The conditions found most suitable for the preparation of this compound were the following. Ten grams of the base were dissolved in dilute hydrochloric acid, and the solution was heated to the boiling point for one minute. It was then cooled, and the crystals of the imide which separated were collected and recrystallised from water. It formed small prisms, melting and decomposing at  $230\text{--}235^\circ$ :

0·1306 gave 0·2540 CO<sub>2</sub> and 0·0711 H<sub>2</sub>O. C = 54·11; H = 5·90.

0·1268 „ 20·3 c.c. N<sub>2</sub> at  $17^\circ$  and 743 mm. N = 18·6.

C<sub>10</sub>H<sub>13</sub>O<sub>3</sub>N<sub>3</sub> requires C = 53·8; H = 5·8; N = 18·8 per cent.

The imide dissolves in dilute sodium carbonate solution. The products formed from it on hydrolysis are the same as those from the piperidone base.



This compound is formed as the ultimate product of hydrolysis of 6-imino-3-cyano-5-carbamyl-4-methyl-4-ethyl-2-piperidone, or the corresponding diketo-derivative, by aqueous potassium hydroxide. Either one or other of these compounds is boiled with an aqueous solution containing rather more than the calculated quantity of potassium hydroxide until the odour of ammonia ceases to be apparent, when the solution is acidified by hydrochloric acid, saturated with ammonium sulphate, and extracted several times with ether. The oily residue left on evaporating the ether is then heated at  $160^\circ$  until the evolution of carbon dioxide has ceased, when the residue, which solidifies on cooling, is recrystallised from water. *ββ*-Methylethylglutarimide forms lustrious plates, which melt at  $127^\circ$ :

0·1446 gave 0·3269 CO<sub>2</sub> and 0·1095 H<sub>2</sub>O. C = 61·72; H = 8·41.

C<sub>8</sub>H<sub>13</sub>O<sub>3</sub>N requires C = 61·9; H = 8·4 per cent.

The imide is sparingly soluble in cold ether, and can be recrystallised from this solvent; it can also be recrystallised from benzene.

The silver salt separates as a colourless precipitate when a little ammonia is added to a solution of the compound in dilute silver nitrate solution:

0·2465 gave 0·1015 Ag. Ag = 41·18.

C<sub>8</sub>H<sub>12</sub>O<sub>2</sub>NAg requires Ag = 41·2 per cent.

*$\beta\beta$ -Methylethylglutaric Acid*,  $\text{CO}_2\text{H}\cdot\text{CH}_2\cdot\text{CMeEt}\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$ .

This acid is produced in quantitative yield when the piperidone base or the corresponding imide is heated with 70 per cent. sulphuric acid. Fifty grams of the base are dissolved in 75 c.c. of concentrated sulphuric acid, and 25 c.c. of water are added to the hot solution. The mixture is then quickly heated on the sand-bath until carbon dioxide begins to be evolved, when it is maintained at this temperature until all gas has been given off. A further 30 c.c. of water are then added, and the heating continued for five hours. If too much water is added in the first instance, a crystalline precipitate of the di-imide separates on heating, and when once this compound has separated, it will not again dissolve. The acid is extracted from the cooled product of hydrolysis by means of ether, and is obtained as a crystalline mass on evaporating the dried ethereal solution. The acid is sufficiently pure for general purposes, but can be recrystallised from a mixture of equal parts of concentrated hydrochloric acid and water, from which it separates in striated, fan-shaped needles. The specimen for analysis was recrystallised from benzene and obtained in long needles, melting at 86°:

0·1794 gave 0·3627  $\text{CO}_2$  and 0·1308  $\text{H}_2\text{O}$ . C=55·10; H=8·11.  
 $\text{C}_8\text{H}_{14}\text{O}_4$  requires C=55·2; H=8·0 per cent.

 *$\beta\beta$ -Methylethylglutaric Anhydride*,  $\text{CMeEt} <\text{CH}_2\cdot\text{CO}>_2\text{O}$ .

This compound may be prepared either by the action of acetyl chloride or acetic anhydride on the acid. Ten grams are dissolved in the dehydrating agent, and heated to the boiling point for one hour. The solution is then distilled, first under ordinary pressure until free from acetic acid, and then under diminished pressure. The anhydride distils as a clear, colourless liquid at 185°/20 mm. It could not be obtained in a solid condition:

0·2477 gave 0·5570  $\text{CO}_2$  and 0·1711  $\text{H}_2\text{O}$ . C=61·25; H=7·72.  
 $\text{C}_8\text{H}_{12}\text{O}_3$  requires C=61·5; H=7·7 per cent.

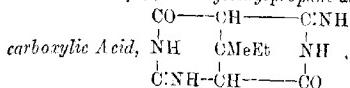
The anhydride slowly dissolves on boiling with water, regenerating the acid from which it was derived.

The  *$\alpha$ -naphthylamic acid*,  $\text{C}_{10}\text{H}_7\cdot\text{NH}\cdot\text{CO}\cdot\text{CH}_2\cdot\text{CMeEt}\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$ , is prepared by boiling a solution of the anhydride in benzene with a solution of  *$\alpha$ -naphthylamine* in the same solvent and evaporating the solution to dryness. The viscous oil which remains solidifies on being rubbed with dilute hydrochloric acid. It crystallises from alcohol in long needles, melting at 126°:

0·1676 gave 0·4416 CO<sub>2</sub> and 0·1060 H<sub>2</sub>O. C=71·81; H=7·00.  
C<sub>17</sub>H<sub>19</sub>O<sub>3</sub>N requires C=71·6; H=6·7 per cent.

Derivatives of the anhydride seem to possess little tendency to crystallise, and the anilic acid from the anhydride and aniline, as well as the toluidic acids from the three toluidines, could only be obtained as oils.

*The Di-imino-di-imide of ββ-Methylethylpropane-ααγγ-tetra-*



As in the case of the compound formed in the acetone condensation, this substance may be prepared from the piperidone base either by the action of sodium ethoxide or by the aid of aqueous sodium hydroxide. In the experiment with sodium ethoxide, 7 grams of the finely ground base were suspended in 25 c.c. of alcohol and mixed with a solution containing 1·5 grams of sodium in 20 c.c. of alcohol. The base dissolved on adding the alkali, forming a yellow solution, from which a colourless, crystalline sodium salt separated on warming. This salt was collected, dissolved in water, and the solution rendered acid by acetic acid, when a copious precipitate of the di-imino-base ensued. The same substance may also be produced in the following way. The piperidone base is dissolved in a sufficient quantity of dilute aqueous potassium hydroxide, and the yellow solution is then gently warmed until the colour is discharged, when it is immediately cooled and rendered acid by acetic acid. The di-imino-base is then precipitated in the pure condition.

It is very sparingly soluble in all the usual solvents, and is therefore best purified for analysis by dissolving in cold dilute hydrochloric acid, and reprecipitating from the filtered solution by the addition of sodium acetate solution. In this way it is obtained in small, colourless needles, which melt and decompose at 294°:

0·1496 gave 32·7 c.c. N<sub>2</sub> at 12° and 726 mm. N=25·1.

0·1494 " 32·4 c.c. N<sub>2</sub> " 13° " 739 mm. N=25·2.

C<sub>10</sub>H<sub>14</sub>O<sub>2</sub>N<sub>4</sub> requires N=25·2 per cent.

It is worthy of remark that several carbon and hydrogen estimations of this substance invariably gave the carbon content as 2 per cent. too low. As the combustions were carried out both in copper oxide and lead chromate tubes, the loss of carbon can be hardly due to the formation of paraffin hydrocarbons, but must be ascribed to incomplete combustion.

The di-imino-di-imide dissolves in aqueous alkali hydroxide, form-

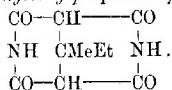
ing a colourless solution, and forms a salt with hydrochloric acid containing two equivalents of the acid.

The *platinichloride* requires some care in preparation, owing to the ease with which the base is hydrolysed to the di-imide even by cold dilute hydrochloric acid. It separates in yellow plates from a concentrated solution of the base, containing as little hydrochloric acid as possible, when it is mixed with an aqueous solution of platinic chloride:

0·4273 gave 0·1333 Pt. Pt=31·19.

$C_{10}H_{14}O_2N_4H_2PtCl_6$  requires Pt=30·9 per cent.

*The Di-imide of  $\beta\beta$ -Methylethylpropane- $\alpha\gamma\gamma$ -tetracarboxylic Acid,*



This compound separates in glistening plates when a solution of the di-imino-base in dilute hydrochloric acid is gently warmed. When prepared in this manner, it is quite free from all impurities, although it may be recrystallised from a considerable quantity of hot alcohol. It melts and darkens at 330—331° (corr.): \*

0·1988 gave 0·3896  $CO_2$  and 0·0935  $H_2O$ . C=53·41; H=5·20.

0·1369 „ 15·0 c.c.  $N_2$  at 13° and 745 mm. N=12·7.

$C_{10}H_{12}O_4N_2$  requires C=53·6; H=5·3; N=12·5 per cent.

The di-imide dissolves slowly in an aqueous solution of sodium carbonate.

*The Silver Salt.*—When silver nitrate solution is added to a solution of the di-imide in excess of ammonia, a white precipitate is formed, which again passes into solution. When the containing vessel is scratched, a crystalline salt separates. Care must be taken in this preparation to have excess of ammonia present; otherwise a gelatinous silver salt separates:

0·1438 gave 0·0467 Ag. Ag=32·47.

$C_{10}H_{11}O_4N_2Ag$  requires Ag=32·7 per cent.

The products formed by the hydrolysis of the di-imino-base and the di-imide are similar to those from the corresponding compounds formed in the acetone condensation. Thus, on complete hydrolysis with aqueous alkali hydroxide,  $\beta\beta$ -methylethylglutarimide is formed, and when they are boiled with concentrated sulphuric acid, a quantitative yield of  $\beta\beta$ -methylethylglutaric acid is obtained. The conditions required are the same as those given in the case of the acetone compounds.

Melting points above 300° were taken in cyanobenzyline (compare Trans., 1906, 20, 1932).

*The Condensation of cycloHexanone with Cyanoacetamide.*

*The ω'-Imino-imide of α-Cyano-α'-carbamylcyclohexane-1: 1-diacetic Acid,*  $\text{CH}_2\left<\begin{matrix} \text{CH}_2 & \text{CH}_2 \\ & \text{CH}_2 \end{matrix}\right>\text{C}\left<\begin{matrix} \text{CH}(\text{CN}) \\ \text{CH}(\text{CO-NH}_2) \end{matrix}\right>\text{CO}\left<\begin{matrix} \\ \text{C}(\text{NH}) \end{matrix}\right>\text{NH}.$

Owing to the insolubility of *cyclohexanone* in water, it is necessary in this condensation to use alcohol in order to bring the reacting substances into solution. Seventy-four grams of cyanoacetamide were dissolved in a sufficient quantity of cold water, and 44 grams of *cyclohexanone*, together with sufficient alcohol to ensure complete solution, added. The addition of 1 c.c. of piperidine or of 1 c.c. of 30 per cent. sodium hydroxide solution caused the liquid to become yellow, and at the end of twelve hours a large quantity of crystalline material had separated. When collected and dried, the product weighed 90 grams, and was found to be completely soluble in dilute hydrochloric acid. A further quantity of crystalline substance separated from the filtrate on keeping, and 8 grams more of the base were obtained on rubbing this with dilute hydrochloric acid, filtering, and adding sodium acetate solution to the filtrate. The base, like the other compounds of this class, is slowly decomposed on boiling with water, and it is therefore best to purify it by dissolving in dilute hydrochloric acid, filtering, and precipitating the base by sodium acetate solution. It is obtained in this way in microscopic needles, which melt and decompose at 305°:

0·1810 gave 0·3841 CO<sub>2</sub> and 0·1050 H<sub>2</sub>O. C=57·93; H=6·51.

0·1183 „ 23·6 c.c. N<sub>2</sub> at 16° and 733 mm. N=22·8.

C<sub>12</sub>H<sub>16</sub>O<sub>2</sub>N<sub>4</sub> requires C=58·1; H=6·4; N=22·6 per cent.

The base is readily soluble in dilute mineral acids, and dissolves in aqueous sodium hydroxide, forming a yellow solution, from which the colour is discharged on warming, a change which is due to the formation of the disodium salt of the di-imino-di-imide. Complete hydrolysis with alkali hydroxide yields the imide of *cyclohexane-1: 1-dimalonic acid*, whilst ultimate hydrolysis with concentrated sulphuric acid furnishes a quantitative yield of *cyclohexane-1: 1-diacetic acid*.

The *platinichloride* separates as a yellow precipitate when a solution of the base in dilute hydrochloric acid is mixed with a solution of platinic chloride:

0·3217 gave 0·0686 Pt. Pt=21·32.

(C<sub>12</sub>H<sub>16</sub>O<sub>2</sub>N<sub>4</sub>)<sub>2</sub>H<sub>2</sub>PtCl<sub>6</sub> requires Pt=21·5 per cent.

As in the former condensations, a small quantity of a second substance, insoluble in dilute hydrochloric acid, is formed during the condensation of *cyclohexanone* with cyanoacetamide. It occurs only in the later stages, and is isolated in the same manner as the

analogous compounds from the previous condensations. It separates from alcohol in small, colourless needles, which melt at 207°. We have not as yet succeeded in assigning any satisfactory constitution to this substance.

*The  $\omega$ -Imide of  $\alpha$ -Cyano- $\alpha'$ -carbamylcyclohexane-1:1-diacetic Acid,*



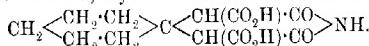
This substance is formed when the base already described is warmed with dilute hydrochloric acid. Ten grams of the base are dissolved in a sufficient quantity of dilute hydrochloric acid, and the solution is then raised to the boiling point and maintained at this temperature for one minute. Crystals of the imide separate on cooling. It can be recrystallised from alcohol, and is obtained in colourless prisms, melting sharply to an opaque liquid at 260°, which clears and decomposes at 300°:

0·1722 gave 0·3639 CO<sub>2</sub> and 0·0926 H<sub>2</sub>O. C=57·73; H=6·04.  
0·1136, " 17·6 c.c. N<sub>2</sub> at 23° and 725 mm. N=17·1.

C<sub>12</sub>H<sub>15</sub>O<sub>3</sub>N<sub>3</sub> requires C=57·8; H=6·0; N=16·9 per cent.

The imide slowly dissolves in sodium carbonate solution. The products formed on hydrolysis are the same as those from the imino-imide.

*The Imide of cycloHexane-1: 1-dimalonic Acid,*

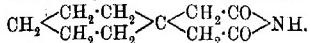


This compound is produced when either the imino-imide or the imide is boiled with aqueous alkali hydroxide. A convenient quantity is dissolved in an aqueous solution containing rather more than the calculated quantity of potassium hydroxide, and boiled until the odour of ammonia ceases to be apparent, when it is filtered and acidified with hydrochloric acid. Crystals of the acid slowly separate, which, when recrystallised from water, yield small needles, melting at 117°; the liquid evolves carbon dioxide a few degrees higher, and then re-solidifies. This change is due to the passage of the dicarboxylic acid into the imide, which melts at 168°:

0·1901 gave 0·3724 CO<sub>2</sub> and 0·0975 H<sub>2</sub>O. C=53·42; H=5·70.

C<sub>12</sub>H<sub>15</sub>O<sub>5</sub>N requires C=53·5; H=5·6 per cent.

The acid is very sparingly soluble in ether.

*The Imide of cycloHexane-1: 1-diacetic Acid,*

The imide-dicarboxylic acid, when heated in a bath of sulphuric acid at 180° until the evolution of carbon dioxide has ceased, leaves the imide as an oily residue, which solidifies on cooling. It crystallises from benzene in large, prismatic needles, which melt at 168°:

0·2186 gave 0·5286 CO<sub>2</sub> and 0·1582 H<sub>2</sub>O. C=66·01; H=8·10.  
C<sub>10</sub>H<sub>15</sub>O<sub>2</sub>N requires C=66·2; H=8·3 per cent.

The imide is very sparingly soluble in ether or water.

The silver salt separates from a solution of the imide in excess of ammonia on the addition of silver nitrate solution as a colourless, crystalline precipitate:

0·3002 gave 0·1120 Ag. Ag=37·30.

C<sub>10</sub>H<sub>14</sub>O<sub>2</sub>NAg requires Ag=37·5 per cent.

*cycloHexane-1: 1-diacetic Acid, CH<sub>2</sub> $\left\langle \begin{matrix} \text{CH}_3 & \text{CH}_2 \\ & \text{CH}_2 \cdot \text{CH}_2 \end{matrix} \right\rangle \text{C} \left\langle \begin{matrix} \text{CH}_2 & \text{CO}_2\text{H} \\ & \text{CH}_2 \cdot \text{CO}_2\text{H} \end{matrix} \right\rangle \text{II.}$* 

The conversion of the  $\omega'$ -imino-imide of  $\alpha$ -cyano- $\alpha'$ -carbamylcyclohexane-1: 1-diacetic acid into the above acid is accomplished, as in the former cases, by the aid of concentrated sulphuric acid. Forty grams of the imino-imide are dissolved in 100 c.c. of concentrated sulphuric acid, and the warm solution mixed with 15 c.c. of water. It is then heated on the sand-bath until carbon dioxide begins to be evolved, when it is kept at about this temperature until all has been given off, which is usually at the end of one hour. A further 50 c.c. of water are then added, and the solution boiled for five hours. If some of the crystalline di-imide separates during the process of hydrolysis, which is always the case if too much water has been added, it is advisable to filter it off through glass wool, as when once it has separated, it will not redissolve on further heating. If, however, the conditions given above are carefully followed, the di-imide will not separate, and the hydrolysis will be complete. Although the acid separates from the sulphuric acid solution on cooling, it is advisable to extract with ether and shake the ethereal solution with aqueous sodium carbonate, the acid being precipitated from the alkaline extract by means of hydrochloric acid.

*cycloHexane-1: 1-diacetic acid* crystallises from dry ether in small, colourless prisms, which melt at 181°. It is sparingly soluble in hot water, but can be recrystallised from this solvent if a sufficient quantity is used. For general purposes it is conveniently

recrystallised from dilute alcohol. It is sparingly soluble in benzene. When distilled under ordinary pressure, it passes into the anhydride, the change being effected without any charring:

0·2159 gave 0·4742 CO<sub>2</sub> and 0·1539 H<sub>2</sub>O. C=59·92; H=7·93.

C<sub>10</sub>H<sub>16</sub>O<sub>4</sub> requires C=60·01; H=8·0 per cent.

A neutral solution of the ammonium salt of the acid gives a green, crystalline precipitate with copper sulphate, a white, crystalline precipitate on boiling with calcium chloride, and a heavy, white precipitate with lead acetate. The barium salt is soluble.

The silver salt separates as a colourless, crystalline precipitate on adding a solution containing the calculated quantity of silver nitrate to a neutral solution of the ammonium salt of the acid:

0·2383 gave 0·1239 Ag. Ag=52·02.

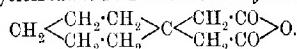
C<sub>10</sub>H<sub>14</sub>O<sub>4</sub>Ag<sub>2</sub> requires Ag=52·2 per cent.

The diethyl ester is formed when a solution of the acid in alcohol is mixed with one-third of its volume of concentrated sulphuric acid, and heated for one hour on the water-bath. It is extracted by pouring the product into water and separating the oil by means of ether, the ethereal solution being subsequently washed with sodium carbonate, dried, and evaporated. The ester distils at 288°/733 mm., without any decomposition, as a clear, mobile liquid:

0·1691 gave 0·4061 CO<sub>2</sub> and 0·1410 H<sub>2</sub>O. C=65·50; H=9·32.

C<sub>14</sub>H<sub>24</sub>O<sub>4</sub> requires C=65·6; H=9·4 per cent.

*cycloHexane-1: 1-diacetic Anhydride,*



This substance is formed either by the action of acetyl chloride or of acetic anhydride on the acid. For the preparation of large quantities, acetic anhydride is preferable, and it is only necessary to boil a solution of the acid in excess of anhydride for two hours and to distil the product in order to obtain the anhydride in a pure condition. It distils without decomposition at 329°/743 mm. and 213°/36 mm. as a colourless liquid, which solidifies on cooling. It then crystallises from a mixture of light petroleum (b. p. 80–90°) and benzene in fine, silky needles, which melt at 73°:

0·2165 gave 0·5230 CO<sub>2</sub> and 0·1436 H<sub>2</sub>O. C=65·91; H=7·45.

C<sub>10</sub>H<sub>14</sub>O<sub>3</sub> requires C=65·9; H=7·7 per cent.

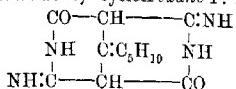
The anhydride dissolves when warmed with aqueous alkali, and the solution, on acidifying, deposits the acid melting at 181°.

The *anilic acid* is prepared by mixing a solution of the anhydride in benzene with a benzene solution of aniline, and raising the mixture to the boiling point. It is isolated by evaporating the

solution until free from benzene, and rubbing the residue with dilute hydrochloric acid. The solid which is then formed crystallises from dilute alcohol in glistening plates, which melt at 146°: 0·1514 gave 0·3864 CO<sub>2</sub> and 0·1045 H<sub>2</sub>O. C=69·60; H=7·71.  
C<sub>16</sub>H<sub>21</sub>O<sub>3</sub>N requires C=69·8; H=7·6 per cent.

The anilic acid is readily soluble in benzene and in alcohol.

*The Di-imino-di-imide of cycloHexane-1:1-dimalonic Acid,*



The methods used for the preparation of this substance were essentially the same as those employed for the production of the similar compounds in the earlier condensations.

*By Sodium Ethoxide.*—12·4 Grams of the base were suspended in 40 c.c. of alcohol and mixed with a solution containing 2·3 grams of sodium in 30 c.c. of alcohol. The yellow solution which was then formed deposited, on warming, a large quantity of a colourless, crystalline sodium compound, which was collected, washed with alcohol, and dried:

0·3762 gave 0·1561 Na<sub>2</sub>SO<sub>4</sub>. Na=13·44.

C<sub>12</sub>H<sub>14</sub>O<sub>2</sub>N<sub>4</sub>Na<sub>2</sub>C<sub>2</sub>H<sub>5</sub>O requires Na=13·6 per cent.

It was not found possible to free the sodium compound from alcohol without causing decomposition. The salt is readily soluble in cold water, and when the solution is rendered acid by acetic acid, a colourless precipitate of the di-imino-base ensues.

*By Alkali Hydroxide.*—When the  $\omega'$ -imino-imide of  $\alpha$ -cyano- $\alpha'$ -carbamylcyclohexane-1:1-diacetic acid is dissolved in a sufficient quantity of aqueous potassium hydroxide, a yellow solution is formed, which, on warming, becomes colourless. If the solution is at this stage rapidly cooled and acidified by acetic acid, the di-imino-base is at once precipitated. The di-imino-di-imide is insoluble in all the usual organic solvents, but can be purified by dissolving in cold dilute hydrochloric acid, and reprecipitating by the addition of sodium acetate solution. It forms a micro-crystalline powder, which melts and decomposes at 303°:

0·1445 gave 28·6 c.c. N<sub>2</sub> at 15° and 726 mm. N=22·5.

C<sub>12</sub>H<sub>14</sub>O<sub>2</sub>N<sub>4</sub> requires N=22·6 per cent.

We were unable to obtain a satisfactory carbon estimation of this compound, for, as in the case of the corresponding compound from methyl ethyl ketone, the figures were always from 1 to 2 per cent. too low.

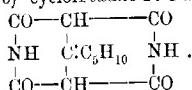
The di-imino-di-imide dissolves in aqueous potassium hydroxide, forming a colourless solution, and gives with hydrochloric acid a salt which contains two equivalents of the acid.

The *platinichloride* separates as a yellow precipitate when a solution of platinic chloride is added to a cold solution of the base in dilute hydrochloric acid:

0·3748 gave 0·1104 Pt. Pt = 29·45.

$C_{12}H_{14}O_2N_4H_2PtCl_6$  requires Pt = 29·6 per cent.

*The Di-imide of cycloHexane-1: 1-dimalic Acid,*



This substance is formed when a solution of the di-imino-base in dilute hydrochloric acid is boiled for one minute, and separates completely from the hot solution. It can be recrystallised from much glacial acetic acid, and separates in small prisms, which melt at 400—405°, partly subliming below that temperature:

0·1904 gave 0·4030  $\text{CO}_2$  and 0·0932  $\text{H}_2\text{O}$ . C = 57·83; H = 5·50.

0·1236 „ 12·0 c.c.  $\text{N}_2$  at 14° and 748 mm. N = 11·45.

$C_{12}H_{14}O_4N_2$  requires C = 57·6; H = 5·6; N = 11·2 per cent.

The di-imide dissolves in a warm solution of sodium carbonate.

The products of hydrolysis of the di-imino-base and the di-imide are the same as those from the corresponding monocyclic compounds. Thus, with alkali hydroxide, the imide of *cyclohexane-1: 1-diacetic acid* is the ultimate product, whilst with concentrated sulphuric acid a quantitative yield of *cyclohexane-1: 1-diacetic acid* is obtained.

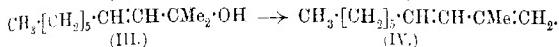
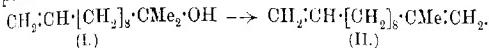
THE SORBY RESEARCH LABORATORY,  
THE UNIVERSITY, SHEFFIELD.

#### LIV.— $\beta$ -Methyl- $\Delta^{\alpha}$ -dodecadiene and $\beta$ -Methyl- $\Delta^{\alpha\gamma}$ -decadiene.

By VICTOR JOHN HARDING, GERTRUDE MAUD WALSH, and  
CHARLES WEIZMANN.

THE compounds described in this communication were prepared with a view to their possible technical importance, and although some of the substances possess some value as perfumes, their pro-

duction by the methods described here render them too costly to permit of their technical application.  $\beta$ -Methyl- $\Delta^{2\alpha}$ -dodecadiene and  $\beta$ -methyl- $\Delta^{2\gamma}$ -decadiene were prepared by the withdrawal of water from the corresponding tertiary alcohols, it being assumed that they possess the constitution indicated:



The tertiary alcohols were obtained by the action of the Grignard reagent on methyl undecenoate and methyl nonenoate respectively. The removal of water from (I) was easily effected by means of phthalic anhydride, but the second alcohol (III), on treatment with any acid dehydrating agent, gave polymerised products of high boiling point, and anhydrous baryta had no action. By allowing the Grignard mixture to remain for twenty-four hours, however, water was eliminated, and the hydrocarbons were obtained, although in extremely poor yield. Another interesting compound, namely, *methyl*  $\theta$ -*aldehydo-n-nonoate*,  $\text{CHO}\cdot[\text{CH}_2]_8\text{CO}_2\text{Me}$ , was obtained by the action of ozone on methyl undecenoate.

#### EXPERIMENTAL.

##### *aa Dimethyl- $\Delta^2$ -undecenyl Alcohol*, $\text{CH}_2\cdot\text{CH}\cdot[\text{CH}_2]_8\cdot\text{CMe}_2\cdot\text{OH}$ .

Fifty grams of magnesium methyl iodide were prepared in ethereal solution in the usual manner, and to the solution were added 30 grams of methyl undecenoate, also in ethereal solution, the flask being kept cold by a stream of water. The product was decomposed by water and hydrochloric acid, the ethereal layer separated, washed with water, and ether removed by distillation. The residual oil was then boiled for ten minutes with alcoholic potassium hydroxide to destroy any unchanged ester, and poured into water. The alcohol, which separated as an oil, was extracted with ether, dried over anhydrous magnesium sulphate,\* and distilled. It is a colourless oil, with a characteristic and rather unpleasant odour, and boils at  $130^\circ/10$  mm.:

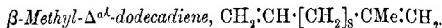
0·1432 gave 0·4134  $\text{CO}_2$  and 0·1718  $\text{H}_2\text{O}$ . C = 78·7; H = 13·3.

$\text{C}_{13}\text{H}_{26}\text{O}$  requires C = 78·8; H = 13·1 per cent.

Determination of the refractive power gave:  $t = 22\cdot2^\circ$ ;  $D_{20}^{20} 0\cdot84217$ ;  $M_\alpha 62\cdot54$ ;  $M^\beta 63\cdot68$ ;  $M_\gamma 64\cdot24$ ;  $M_\gamma - M_\alpha = 1\cdot7$ ;  $(M = \frac{k^2 - 1}{k^2 + 2} p)$ .

\* For drying alcohols in ethereal solution it has been found that anhydrous magnesium sulphate is much preferable to the more commonly used sodium sulphate.

450  $\beta$ -METHYL- $\Delta^{\alpha\alpha}$ -DODECADIENE AND  $\beta$ -METHYL- $\Delta^{\alpha\gamma}$ -DECADIENE

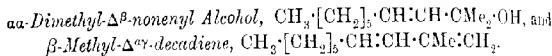


This hydrocarbon is easily and quantitatively prepared from the above-mentioned alcohol by boiling it with the theoretical quantity of phthalic anhydride for four hours. The mixture is then poured into a dilute solution of sodium carbonate, the hydrocarbon extracted by means of ether, and distilled, when it passed over at 150—155°/67 mm. On redistillation over metallic sodium, the hydrocarbon boiled at 152°/67 mm.:

0·1267 gave 0·3999  $\text{CO}_2$  and 0·1518  $\text{H}_2\text{O}$ . C=86·1; H=13·3.

$\text{C}_{13}\text{H}_{24}$  requires C=86·6; H=13·3 per cent.

$\beta$ -Methyl- $\Delta^{\alpha\alpha}$ -dodecadiene is a colourless oil with a faint, lemon-like odour.



Both these substances can be prepared by the interaction of magnesium methyl iodide and methyl  $\Delta^\alpha$ -nonenoate (compare Harding and Weizmann, Trans., 1910, 97, 299). To prepare the alcohol, methyl  $\Delta^\alpha$ -nonenoate is added to the theoretical amount of magnesium methyl iodide in ethereal solution. After two hours the product is worked up in the usual way. The yield is about 30 per cent. of the theoretical. The alcohol boils at 88—90°/10 mm., and possesses an odour resembling that of *n*-nonaldehyde:

0·1325 gave 0·3778  $\text{CO}_2$  and 0·1514  $\text{H}_2\text{O}$ . C=77·7; H=12·7.

$\text{C}_{11}\text{H}_{22}\text{O}$  requires C=77·6; H=12·9 per cent.

Determination of refractive power gave:  $t=17\cdot7^\circ$ ;  $D_4^{20}=0\cdot8265$ ;  $M_a$  54·38;  $M_b$  55·46;  $M_y$  55·92;  $M_y - M_a = 1\cdot54$ .

The compound can be boiled unchanged over anhydrous baryta, but when treated with dehydrating agents, such as phthalic anhydride, zinc chloride, or potassium hydrogen sulphate, polymerised products of high boiling point are obtained.

$\beta$ -Methyl- $\Delta^{\alpha\gamma}$ -decadiene is obtained if the mixture of methyl  $\Delta^\alpha$ -nonenoate and magnesium methyl iodide is allowed to remain for twenty-four hours. The yield is, however, extremely poor. The hydrocarbon is purified by repeated distillation over sodium, and boils at 184°:

0·1831 gave 0·5802  $\text{CO}_2$  and 0·2091  $\text{H}_2\text{O}$ . C=86·2; H=12·7.

$\text{C}_{11}\text{H}_{20}$  requires C=86·8; H=13·1 per cent.

By the interaction of magnesium methyl iodide and methyl crotonate under similar conditions, a small quantity of ethyl alcohol was obtained, and a second fraction, distilling at 122—124°, con-

sisted of methylethylisopropylcarbinol. (Found, C=72·5; H=14·4. Calc., C=72·4; H=13·8 per cent.)

Determination of the refractive power in ethyl-alcoholic solution gave  $t = 20\cdot4^{\circ}$ ;  $\bar{N}_D^{20/4} = 0\cdot8101$ ;  $M_a$  of solute = 36·41.

*Methyl θ-Aldehydo-n-nonoate*,  $\text{CO}_2\text{Me} \cdot [\text{CH}_2]_8 \cdot \text{CHO}$ .

This aldehyde was prepared by passing a current of ozonised oxygen through a solution of methyl undecenoate in chloroform, covered by a layer of water, until the ozone ceased to be absorbed. The chloroform solution was then shaken with a solution of sodium hydrogen sulphite, and the sodium hydrogen sulphite compound, which separated out after some time, collected, washed with ether, and freed from the remainder of the adhering oil by porous porcelain. The colourless, lustrous solid was then distilled in a current of steam from very dilute sodium carbonate solution, and the small amount of oil which passed over was converted into the semicarbazone, which crystallised from alcohol in small needles, melting at 94–96°:

0·1309 gave 0·2735  $\text{CO}_2$  and 0·1066  $\text{H}_2\text{O}$ . C=57·0; H=9·0.

$\text{C}_{13}\text{H}_{25}\text{O}_3\text{N}_3$  requires C=57·6; H=9·2 per cent.

The aldehydo-acid, which possesses a very agreeable, fruity odour, was liberated from its semicarbazone by warm dilute hydrochloric acid.

THE UNIVERSITY,  
MANCHESTER.

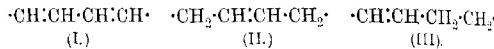
I.V.—*The Influence of Conjugated Linkings on General Absorptive Power. Part I. The Absorption Spectra of Some Benzene Derivatives.*

By CECIL REGINALD CRYMBLE, ALFRED WALTER STEWART,  
ROBERT WRIGHT, and WILLIAM GERALD GLENDINNING.

WHEN an attempt is made to classify the various types of absorption spectra, the first distinction which is drawn is between what is termed general absorption and selective absorption: that is, compounds are divided into those which show a banded absorption spectrum and those which, showing no banded absorption, merely allow more and more of the spectrum to pass through their solutions as the latter are diluted. At the first glance, these two types appear to be quite distinct from one another, but further consideration will show that general absorption may be merely a

special case of selective absorption in which the apparatus devised up to the present is not sufficiently sensitive to detect the other side of the band. For instance, the ordinary photographic plate is sensitive up to a frequency of between four and five thousand; but if the head of a band in any substance lay beyond this region, we should have no means of determining its position, and consequently we should assume that the substance in question gave merely general absorption. The only method which seems likely to throw light on the problem is to study the influences which affect general and selective absorption with a view to correlate the two types. The present paper represents an attempt to determine the influence of unsaturated groupings in the molecule on general absorption.

It was shown by Thiele (*Annalen*, 1899, **306**, 87) that the grouping (I), on reduction, yielded a grouping (II), and not, as was expected, the grouping (III).



and to explain this he put forward his "partial valency" hypothesis, in which he assumed that the affinities of the carbon atoms on either side of the double bonds are not completely saturated, but that there remain partial valencies which, remaining free, are ready to attach themselves to fresh atoms outside the system. The two partial valencies on either side of the central single bond are supposed mutually to saturate each other and thus become temporarily inactive.

It has been shown by Brühi (*Ber.*, 1907, **40**, 878) that such a grouping has a strong influence on refractive power, producing higher values than the calculated refractivity. Hilditch (*Trans.*, 1909, **95**, 331, 1570, 1578; 1910, **97**, 1091; Edminson and Hilditch, *ibid.*, 1910, **97**, 223) has traced the same influence in the case of optically active substances. Analogous results were observed by Pascal (*Compt. rend.*, 1909, **149**, 342) in the case of diamagnetic power. Sir W. H. Perkin (*Trans.*, 1896, **69**, 1141) proved that a similar effect was noticeable in the case of magnetic rotation. One of the present authors, in conjunction with Professor Baly, drew attention to the fact that two conjugated carbonyl groups had a very marked influence on absorption spectra, an absorption band being developed in the spectra of compounds which contain such a grouping.

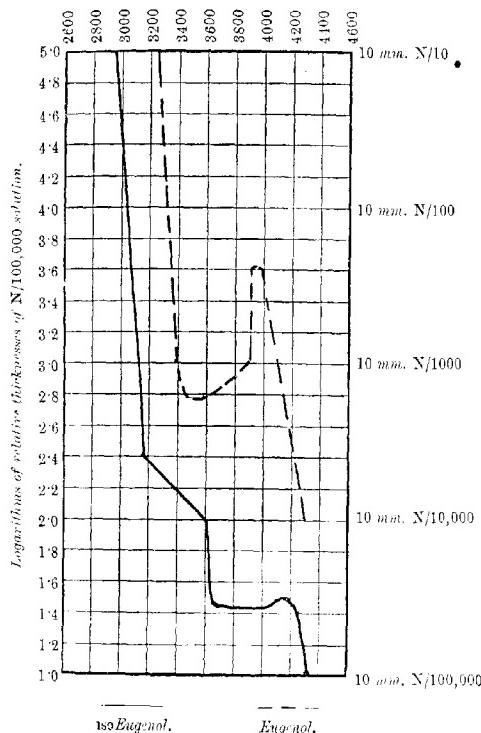
Bearing the foregoing in mind, it seemed desirable to turn to the question of general absorption and examine the spectra of various isomerides which contained systems of one or more conjugated double bonds, with a view to determine the effect which

the presence of the conjugation produced on the absorptive power of the substances. The present paper contains an account of the investigation of some benzene derivatives.

It is clear that comparisons can only be made between two sets

FIG. 1.

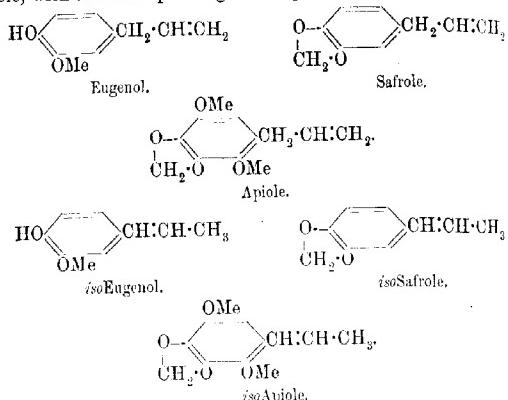
Oscillation frequencies.



of isomeric substances; since the carbon atom in itself appears to exert a certain absorptive power, it would not be proper to compare the general absorptions of two substances one of which contained more atoms than the other.

In the first place, we may consider a group of six compounds

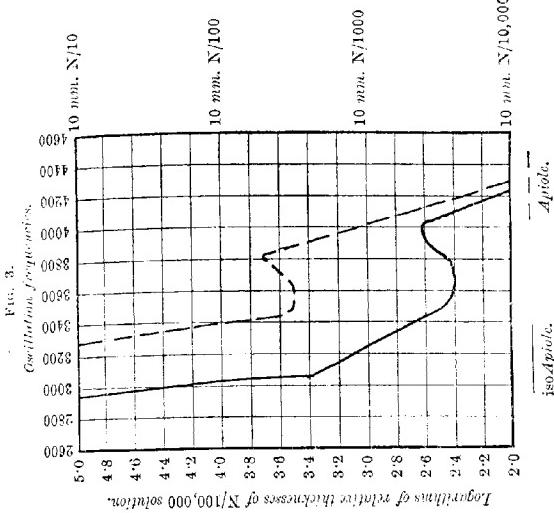
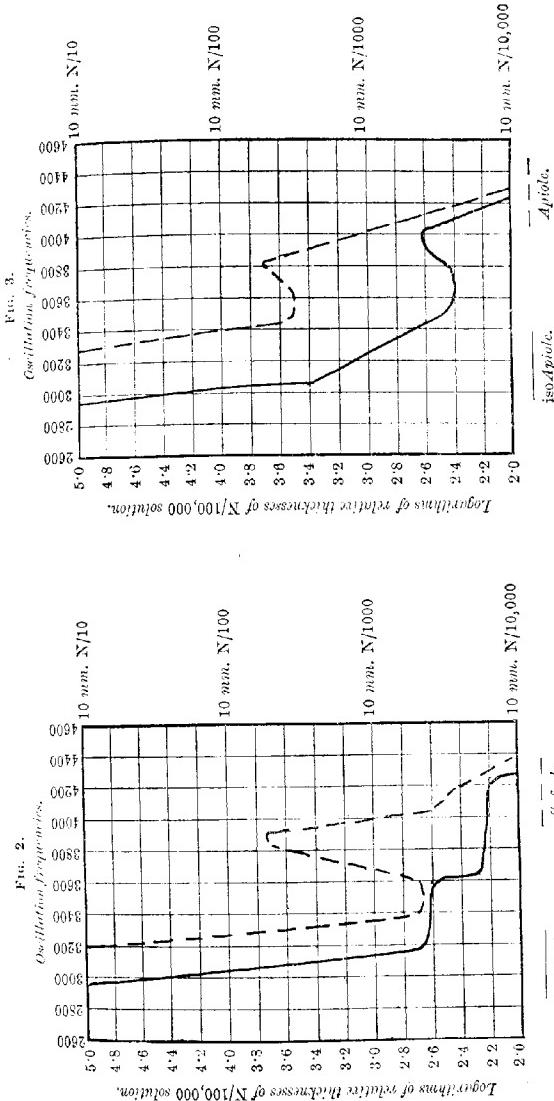
which are closely allied to one another, namely, eugenol, safrole, and apiole, with the corresponding *iso*-compounds (see Figs. 1, 2, and 3):



An examination of the six formulæ above will show that in the case of eugenol and its analogues the double bonds in the side chains are not conjugated with the benzene nuclei; in the case of *iso*eugenol and its congeners, on the other hand, an extra conjugation is introduced, for the double bond in the side chain has been brought nearer to the benzene nucleus, and is now part of the conjugated system.

Turning now to the curves, we must make a selection of the particular region of the spectrum which we propose to examine. As we are dealing with general absorption, it is quite evident that we should not examine the portion of the spectrum which forms part of an absorption band, but that we must deal with some section which lies sufficiently far away from the banded region to be secure from interference on the part of factors which exert influence on selective absorption. If we choose the region lying between 10 mm. of  $N/10$  and 10 mm. of  $N/100$ , we shall avoid the bands which appear in these thicknesses of  $N/1000$  and more dilute solutions.

Inspection of the six curves will show that in every case the compound containing the system of four conjugated double bonds has a greater absorptive power than that which only contains three. This assumes that the benzene nucleus contains a system of three conjugated double bonds, but the conclusion is equally true if we consider the benzene system simply as a reservoir of residual affinity, for in that case we have the two unsaturated systems (nucleus and double bond) separated in eugenol and its



analogues, but conjugated together in *iso*eugenol, *iso*safrole, and *iso*apiole.

Let us next turn to the case of the two substances, acetophenoneoxime and acetanilide (see Fig. 4). Here again we have the benzencoid nucleus in each case, but in acetophenoneoxime we have an extra-nuclear conjugation provided by the group  $\cdot\text{C}:\text{NOH}$  which is absent in acetanilide, the carbonyl group in the latter substance being separated from the nucleus by the interposition of the imino group:



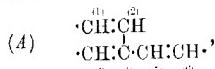
As can be seen from the curves, the rule holds in this case also, for the absorptive power of acetophenoneoxime is much greater than that of acetanilide.

Another example of the same rule is to be found in the cases of phenyl acetate and methyl benzoate:



In the first substance, we have no conjugation apart from that comprised within the benzene system, but in methyl benzoate we have the carbonyl group conjugated with the nucleus. An inspection of the curves in Fig. 5 will show that methyl benzoate has an absorptive power greater than that of the isomeric substance.

We now come to two pairs of isomerides which form a crucial test of this hypothesis. It will be remembered that in his original paper on the partial valency hypothesis (*Annalen*, 1899, **306**, 111) Thiele considered the case of what he termed "crossed double bonds," and showed that in a system of the following type:

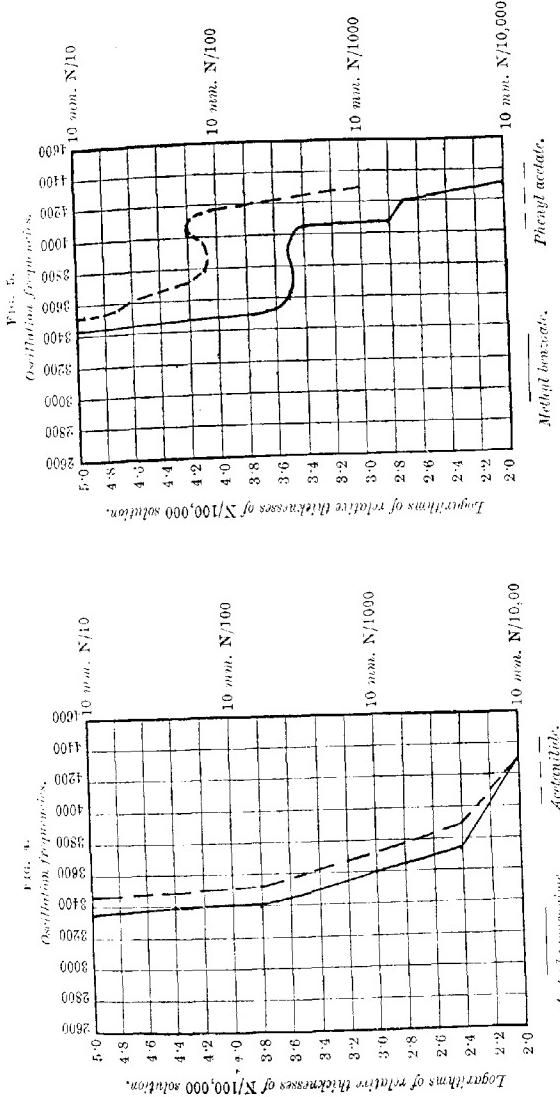


one end of the double bond between the atoms 3 and 4 is conjugated with both the other double bonds. Now, if this be so, it is clear that such a system cannot be regarded as conjugated to the same extent as a system of double bonds, such as:

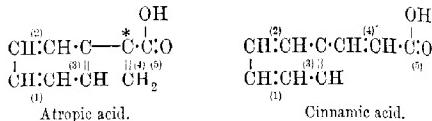


in which the partial valencies neutralise one another in the ordinary manner, leaving only one partial valency free at each end of the system.

In system (A) the partial valency of the atom (4) would have to neutralise not only the partial valency of the atom (2), but also that of the atom (5), and it is clear that in such a case as this we have incomplete conjugation. Such an instance is provided

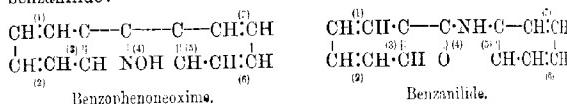


by atropic acid, for in it the double bond of the group  $\text{C}\text{H}_2$  is conjugated with the double bond of the carbonyl group, and also with the nucleus. Compare this with the isomeric cinnamic acid:

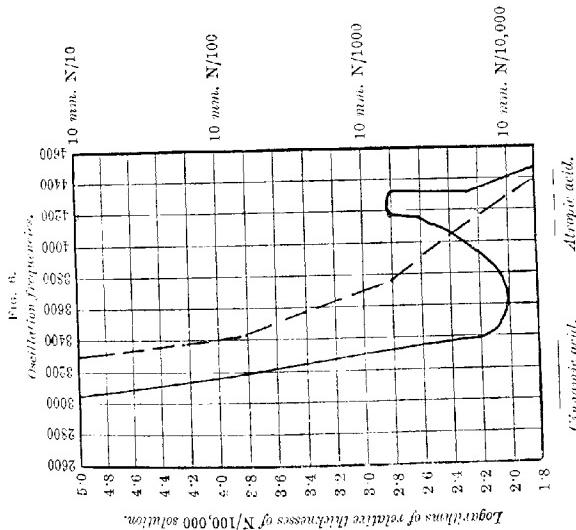
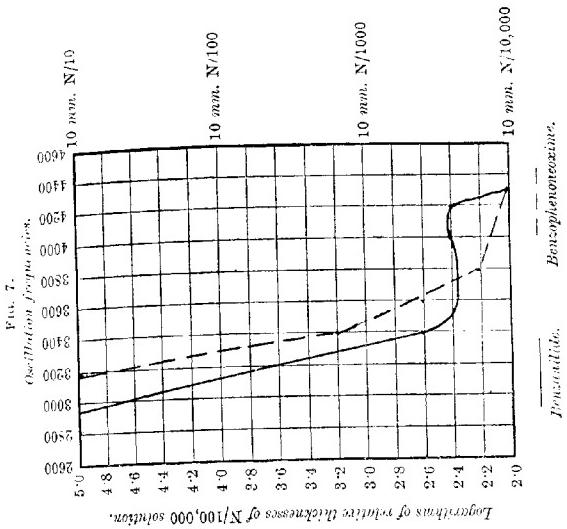


In cinnamic acid, the whole five double bonds form a single conjugated system, whereas in atropic acid, if we regard the first four as a conjugated system, it is clear that the fifth double bond will act as a disturbing influence, tending to absorb some of the partial valency of the atom marked with an asterisk, all of which ought to be devoted to saturating the partial valency of the atom of the benzene ring to which it is attached. It is clear therefore that in cinnamic acid we have a complete system of conjugation, including within itself all the double bonds of the molecule, whereas in atropic acid we have two conflicting systems, and we should therefore expect to find that the absorption of cinnamic acid was more powerful than that of atropic acid. A glance at Fig. 6 will show that this view is correct.

An analogous case is to be found in benzophenoneoxime and benzanilide:



Here the double bond of the group  $\cdot\text{C}(\text{NOH})\cdot$  is conjugated with one double bond in each of the nuclei, whilst in benzanilide no such system of crossed double bonds exists, but, instead, we have two separate systems of conjugation. In both substances we have the same number of double bonds, namely, seven, but whilst in benzanilide we have the double bonds 1, 2, 3, and 4 forming a complete and self-contained conjugated system uninfluenced by the bonds 5, 6, and 7 of the second nucleus, in benzophenoneoxime we have the conjugated system of 1, 2, 3, and 4 disturbed by the intrusion of the bond 5. Thus, in benzophenoneoxime, although we have the same number of double bonds as in benzanilide, their distribution is such as to prevent the complete neutralisation of the partial valencies which is found in true conjugated systems except at their ends. From this, we should expect to find that benzanilide, having most true conjugation in its molecule, had the greater absorptive power, and an inspection of Fig. 7 will show that this is the case.

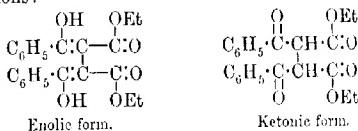


In a set of curves published by Baly and Tuck (Trans., 1906, 89, 982) we have noticed half-a-dozen other examples of this general rule. It is known that when the phenylhydrazones of aldehydes or ketones are exposed to light, they tend to change into azo-compounds. Taking the case of acetaldehydephenylhydrazone as an example, the structures of the two substances are:



It will be seen that in the first compound the double bond  $\cdot\text{N}:\text{CH}\cdot$  is not conjugated with the nucleus, whereas after exposure to light the nucleus is conjugated with the double bond  $\text{N}=\text{X}$ . An examination of the curves given by Baly and Tuck shows that the "conjugated isomeride" has greater absorptive power than the unconjugated hydrazone.

A final instance may be adduced in favour of our views. It has been shown by Hartley and Dobbie (Trans., 1900, 77, 498) that the general absorptive power of the enolic form of ethyl dibenzoyl succinate is much greater than that of the ketonic modifications. A layer of 25 mm. thick of a solution containing one milligram-molecule of the enolic variety in 100 c.c. of alcohol cuts off all rays beyond a frequency of 2171, whereas a corresponding experiment with the ketonic isomeride showed that light is transmitted up to a frequency of 2795. Thus the absorptive powers of the two substances differ by no less than six hundred units under these conditions:



Inspection of the two formulae will show that in the ketonic form the only conjugation is that between the nuclei and the adjacent carbonyl radicles; the two carbonyl groups of the carboxyl radicles are not in conjugation with any double bonds. In the enolic form, on the other hand, the carbonyl radicles of the carboxyl groups are drawn into the general system of conjugation. Thus, in the ketonic form, we have the conjugation of nucleus and  $\text{CO}_2$ -group occurring twice, whilst in the enolic form we have the conjugation of nucleus, ethylenic bonds and carbonyl radicle occurring twice. The latter system is probably weakened by the cross-conjugation of the two ethylenic bonds with each other, but even after deducting a considerable amount for this, we are left with a marked preponderance of conjugation in the enolic and more absorptive form of the substance.

Results similar to those which we have described above have been obtained by us in the alicyclic and open-chain compounds also, and these will furnish the basis of a future paper. The data in the present paper include fourteen pairs of isomerides of the most different types; and we believe that it is established that if we examine two isomeric substances, that which contains the greater number of true conjugated bonds within the molecule will show the greater power of general absorption. These results seem likely to be of interest in the case of terpenes containing two double bonds the relative positions of which have not been definitely established, as a comparison of their general absorptive power with that of isomeric substances of known constitution would enable us to decide whether or not the terpenes in question contained conjugated or unconjugated linkings. We might also mention that in the course of this work we have observed another relation which appears to be general. If the absorptive power of two isomeric substances, one of which is capable of conversion into the other, be examined, we have found that the stable isomeride shows greater absorptive power than the labile form, for example, *n*-propyl bromide has less absorptive power than *isopropyl* bromide, into which it can be converted by heating. This rule holds in those cases where there is no conjugated system in the molecule.

#### EXPERIMENTAL.

*Eugenol*.—This substance was obtained from Kahlbaum, and was purified by fractionation under diminished pressure.

*isoEugenol*.—This was obtained from Kahlbaum, and was twice distilled, the fraction boiling at 167°–168° being finally taken.

*Safrole*.—This was obtained from Kahlbaum, and was re-distilled until it had the correct boiling point.

*isoSafrole*.—Obtained from Kahlbaum. On re-distillation, the middle fraction boiled absolutely constant at 251°, 760 mm.

*Apiole*.—This was purchased from Schuchardt. It had the correct melting point.

*isoApiole*.—This also was obtained from Schuchardt. It was re-crystallised from aqueous alcohol until it melted at 56°.

*Acetophenonearime*.—This was prepared by one of us, and recrystallised from light petroleum until it melted sharply at 59°.

*Acetanilide*.—This was a Kahlbaum specimen, purified in the usual way (m. p. 113°). Two separate specimens of the oxime and the anilide were prepared and photographed, the spectra being found to be identical.

*Methyl Benzoate*.—This substance was prepared by one of us by the action of benzoic chloride on methyl alcohol. It was

fractionally distilled several times, and the fraction boiling constantly at  $199^{\circ}/756$  mm. was used.

*Phenyl Acetate*.—This was prepared by one of us from acetyl chloride and phenol. It was purified until it boiled constantly at  $195.8^{\circ}/756$  mm.

*Cinnamic Acid*.—Part of the curve of this substance had already been published by one of us (Stewart, Trans., 1907, 91, 202). The compound was re-photographed at higher concentrations, and the two curves were found to be coincident.

*Atropic Acid*.—A specimen obtained from Schuchardt (m. p.  $106.5^{\circ}$ ).

*Benzophenoneoxime*.—Prepared in the usual manner. Recrystallised from aqueous alcohol until it had the correct melting point.

*Benzanilide*.—This was obtained from Kahlbaum, and purified by recrystallisation from alcohol.

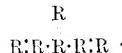
#### Conclusions.

1. The following rule regarding general absorption has been established. Of two isomeric substances containing two or more double bonds, the compound the molecule of which contains the longest chain of conjugations will have the greater absorptive power in the region of the spectrum above that in which any absorption bands make their appearance.

2. In the case where two isomeric substances contain the same number of double bonds, it appears that the compound containing three conjugated groups in a single system:



will have an absorptive power greater than one containing a system of so-called "crossed double bonds":



3. As this rule has been found to hold good in the case of alicyclic substances as well as in the benzene and aliphatic series, it furnishes a possibility of obtaining additional evidence of the structure of terpenes containing two double bonds the relative positions of which are not established.

In conclusion, we desire to thank the Research Fund Committee of the Society for a contribution towards the expenses of this research.

THE SIR DONALD CURRIE LABORATORIES,  
THE QUEEN'S UNIVERSITY OF BELFAST.

*Nl.—The Occlusion of Hydrogen by the Palladium-Gold Alloys.*

By ARTHUR JOHN BERRY.

THE numerous investigations which have been carried out on the occlusion of hydrogen by palladium favour the view that the process consists of the solution of the gas in the metal rather than of chemical combination. Hoitsema (*Zeitsch. physikal. Chem.*, 1895, **17**, 1), in a very complete investigation of the vapour pressure of "palladium-hydrogen," concluded that two immiscible solid solutions are formed. At the same time, the precise nature of the product can scarcely be regarded as completely established.

It appeared to be of interest to investigate the absorption of hydrogen by palladium when alloyed with another metal. The palladium-gold alloys were selected for this purpose. These alloys form a complete series of mixed crystals according to Ruer (*Zeitsch. anorg. Chem.*, 1906, **51**, 391).

In a paper entitled "Additional Observations on Hydrogenium," Graham (*Proc. Roy. Soc.*, 1869, **17**, 500) described some experiments on the occlusion of hydrogen by some alloys of palladium. His results with the palladium-gold alloys in general differ very considerably from those of the present author. These results are discussed at the end of this paper.

EXPERIMENTAL.

The palladium was prepared by the reduction of the chloride by sodium formate in hot aqueous solution. After washing, the spongy metal was fused in the oxy-coal-gas flame, annealed, and rolled.

The alloys were prepared by fusing the two metals in the requisite proportions in the oxy-coal-gas flame on cupels. The buttons were then annealed and rolled, and the whole process repeated to ensure homogeneity of the product.

The occlusion experiments were conducted in the following manner. Two similar voltameters containing dilute sulphuric acid were connected together in series. The cathode of one voltameter was of the alloy the occluding power of which was under investigation. The cathode of the other voltameter, as well as the anodes of both voltameters, were of platinum. The hydrogen evolved from both cathodes was collected in measuring tubes in the usual manner. Since the same current flowed through both voltameters, the quantities of hydrogen liberated at the two cathodes were identical. The amount of hydrogen occluded by the palladium

alloy was simply measured by the difference between the  $\frac{1}{2}v_0$  volumes of gas.

In these experiments, quantities of alloy of 0·5 to 1 gram were employed. Electrolysis was always continued for some time after the alloy appeared to be supersaturated with gas, in order to allow sufficient time for the gas to diffuse inwards. The apparatus was then allowed to stand for several hours before reading the volume of gas. Thoma (*Zeitsch. physikal. Chem.*, 1889, **3**, 69) has shown that palladium can be supersaturated with hydrogen when charged electrolytically; the excess of gas is, however, evolved after the current ceases.

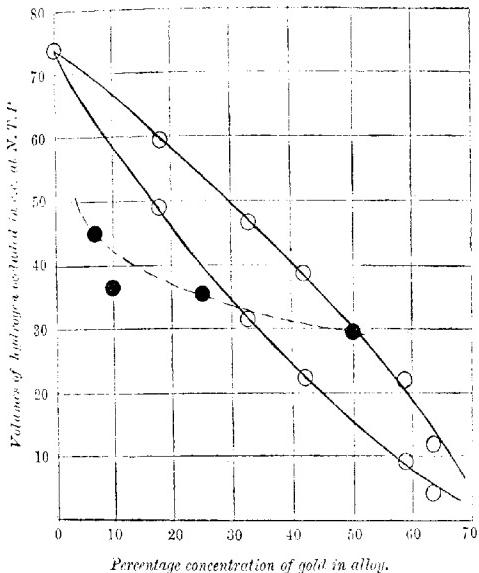
Preliminary experiments gave somewhat inconsistent results for the quantity of hydrogen occluded, and, in general, the more dilute the alloy was in respect to palladium, the greater was the difficulty in obtaining consistent results. It was subsequently found that the inconsistent results were due to incomplete annealing of the alloys before saturating them with hydrogen. Consistent results were readily obtained by annealing the alloys in an electric furnace for about two hours at a temperature of  $650^{\circ}$  before charging them with hydrogen. That the occluding power of palladium depends to some extent on the physical condition of its surface has been noted by several investigators; Mond, Ramsay, and Shields (*Phil. Trans.*, 1898, **A**, **191**, 105) have, however, shown that when the proper conditions are observed, the amount of hydrogen occluded is in all cases approximately the same.

The results are shown in the adjoining diagram. It is clear that the occluding power of alloys containing more than about 25 per cent. of palladium is a simple function of the concentration of that metal, although not simply proportional to it. For comparison the writer has inserted the values obtained by Graham. It is clear that, with the exception of the alloy containing 75·2 per cent. of palladium, the two curves show no agreement. With regard to the alloy containing 50 per cent. of either constituent, Graham remarks as follows (*loc. cit.*): "The presence of so much gold as half its weight did not materially reduce the occluding power of palladium. Such an alloy was capable of occluding 459·9 times its volume of hydrogen with a linear expansion of 1·67 per cent." Graham does not appear to have performed any experiments with alloys more dilute in respect to palladium. For this reason, the present author is of opinion that Graham's results must not be accepted without reserve.

In order to determine whether alloys containing less than 25 per cent. of palladium were capable of occluding hydrogen, an alloy containing 19·5 per cent. of this metal and 80·5 per cent. of gold

was specially prepared. Experiments were made with 4.1745 grams of this alloy instead of with the smaller quantities hitherto employed. In no case was there any evidence of any occlusion having taken place.

The curve appears to be of the general form to be expected for the diminution of the solubility of a substance when the solvent contains increasing quantities of an inert diluent. The question as to why occlusion should cease altogether when the concentration



Upper curve: Occlusion per gram of palladium.  
Lower " : " alloy.  
Broken curve and black points: Graham's results p. r. gram of alloy.

of the palladium falls below about 25 per cent. does not appear to be obvious. It would be premature to attempt to frame any hypothesis to explain this phenomenon at present. It is intended to investigate the occluding properties of other alloys of palladium, and it is hoped that some light may be thrown on the matter.

Before concluding this paper, the writer desires to call attention to some experiments performed by Shields (*Proc. Roy. Soc. Edin.*, 1898, **22**, 169) on the electromotive force of the combination:

## 466. PARTINGTON: THE DETERMINATION OF THE DISSOCIATION

palladium containing much hydrogen, dilute sulphuric acid, palladium containing little hydrogen. Shields calculated the electromotive force of such a cell from the well-known equation:

$$E = \frac{RT}{ne} \log_e \frac{p}{p'}$$

Experiment, however, showed that the electromotive force of the system approximated to zero, and Shields concluded that since the system apparently did not behave as a true concentration cell, a definite compound of palladium and hydrogen was formed. In calculating the electromotive force of the combination, Shields apparently assumes that the ratio of the concentrations of the hydrogen in the concentrated and in the dilute solutions is proportional to the ratio of the osmotic pressures of the hydrogen. This assumption appears to be quite unjustifiable, and, indeed, there is definite experimental evidence against it. An examination of Hoitsema's curves (*loc. cit.*) will show that the vapour-pressure curve at the ordinary temperature continues almost horizontal to the concentration axis throughout the greater part of its range, after which it rises rapidly. It is almost certain that Shields' experiments were performed on the horizontal part of the curve, and if we assume that the vapour pressure is a measure of the osmotic pressure of the hydrogen, an electromotive force approximating to zero is precisely what one would expect. Consequently, this phenomenon cannot be regarded as evidence in favour of the view that palladium and hydrogen form a definite compound.

The author desires to express his sincere thanks to Professor Pope for suggesting the subject of this investigation to him, and for allowing him the use of the palladium chloride for the preparation of the alloys, and to Mr. Heycock for the interest he has taken in these experiments and for his valuable suggestions.

UNIVERSITY CHEMICAL LABORATORY,  
CAMBRIDGE.

**LVII.—*The Determination of the Dissociation Pressures  
of Hydrated Salts by a Dynamical Method.***

By JAMES RIDDICK PARTINGTON.

PROBABLY no branch of physico-chemical investigation has aroused a more lively and sustained interest than that dealing with the dehydration of the so-called molecular compounds of water with substances which are electrolytically dissociated in aqueous solution

—the hydrated salts. The study of this phenomenon by the measurement of the pressure of water vapour in contact with the partly dehydrated salt has claimed the attention of many investigators, and a rich store of numerical data has been amassed. The experimental methods employed may be classified into:

(1) *Statical Methods*, depending on a determination of the pressure of water vapour which has been kept in contact with partly dehydrated salt for a comparatively long time, and including the *Tensimetric Method*, introduced by Mitscherlich, in which the pressure is recorded directly by a gauge, and the *Dew-point Method* of Lescour, in which the pressure is determined by the temperature of a surface on which the vapour deposits dew.

The fact, first asserted by Wiedemann (1866), that such a pressure is definite for a given pair of solid phases, and is a function of the temperature alone, may be regarded as established, although some earlier workers (Precht and Kraut, *Annalen*, 1875, **178**, 129; A. Naumann, *Ber.*, 1874, **7**, 1573) were inclined to believe that they had evidence that this was not the case.

(2) *Dynamical Methods*, of which three types have been utilised:

(i) *The Diffusion Method*, of Müller-Erzbach, in which the vapour formed from the hydrate at the bottom of a cylindrical tube is allowed to diffuse up and out of the tube. The loss in weight after a given time, and the loss in weight of a similar tube containing water, provide the data required.

(ii) *The Transpiration Method*, in which the water removed from the hydrate by a slow stream of air is determined. From this, the vapour pressure may be calculated, on the assumption that water vapour under this pressure obeys the gas laws, either by measuring the volume of air aspirated, or by comparing the weight of water vapour carried away from the hydrate with that carried off from pure water by the same volume of air.

(iii) *Linebarger's Method*, depending on the change of boiling point of a solvent which dissolves water only sparingly, by the introduction of hydrated salt.

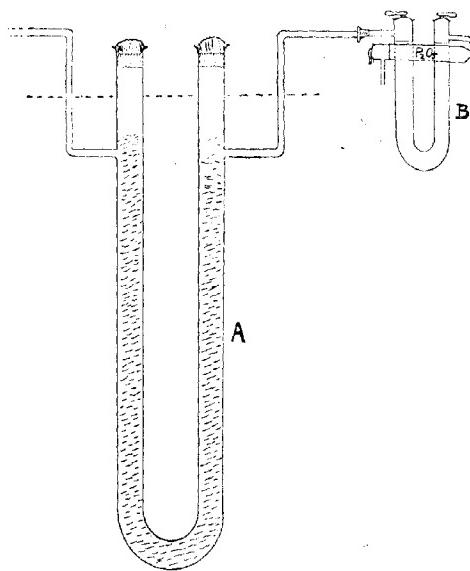
The transpiration method appears to have been used in one research only, namely, by Tammann (*Wied. Ann.*, 1888, **33**, 329), who measured the volume of air passed over the hydrate. He observed that dissociation pressures measured in this way are appreciably higher than those determined tensimetrically. The difference he explained as due to the presence of traces of saturated solution retained by the crystals. H. Schottky (*Zeitsch. physikal. Chem.*, 1908, **64**, 433) has carried out a series of tensimetric measurements with great care, and has observed a similar abnormally high pressure during the initial stages of a static measurement.

He adopted Tammann's explanation: "Schwer zu vermeiden war ferner eine Störung, die wohl der Adsorption, dem Festhalten einer Lösungshaut an den grossen Oberflächen der gepulverten Salze, zuzuschreiben ist. Nach frischer Beschickung des Apparates traten zunächst viel zu grosse Drucke auf."

#### EXPERIMENTAL.

The author has carried out a number of experiments by the transpiration method, but instead of measuring the volume of air

FIG. 1.



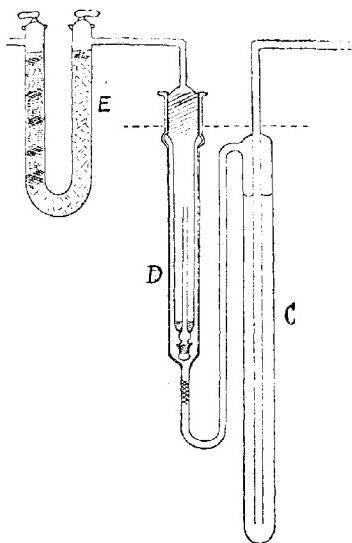
aspirated through the apparatus, which involves troublesome corrections for changes of barometric pressure, the air, after passing over the hydrate, was allowed to bubble through water at the same temperature. If  $w_1, w_2$  are the weights of water removed from the hydrate and pure water respectively, at any temperature  $\theta$ , it is easily shown that:

$$\rho_\theta = \frac{w_1}{w_2} \pi_\theta, \dots \dots \dots \quad (1)$$

where  $p_0$ ,  $\pi_0$  are the dissociation pressure of the hydrate and the vapour pressure of water respectively, with the same assumption as before.

Two forms of apparatus were used, the first (Figs. 1 and 2) for low temperatures ( $20^\circ$ ,  $25^\circ$ ). The hydrate was contained in the U-tube  $A$ , which was 30 cm. in height and 2 cm. in diameter. This was closed by well-paraffined corks covered outside with soft wax, and was connected on one side with a series of drying towers and a small gas meter, on the other with an absorption tube  $B$ ,

FIG. 2.



containing calcium chloride and phosphoric oxide. Ground-glass joints, covered with a thin layer of vaseline, were used for connecting all parts of this and the second apparatus, in which water vapour was present. Rubber connexions and stoppers are quite useless in such cases, on account of their hygroscopic nature. The tube  $B$  was connected through a protective drying tube by a piece of lead tubing and rubber pressure-tubing joints with the water-bubbler  $C$ , a plain glass washing-tube, 20 cm. long and 2 cm. in diameter, which communicated with a trap  $D$ , in which fitted, by a ground joint, the absorption tube  $E$ , containing calcium chloride

and phosphoric oxide. A little glass wool was placed in the tube between *C* and *D*. The tube *E* was connected, through a small wash-bottle containing frequently renewed concentrated sulphuric acid, with two large empty bottles with regulating taps, and these, finally, were attached to a water-pump.

The absorption tube *E*, closed below with a ground cap, was placed in the trap *D* for about five minutes before the commencement of every experiment, so as to assume the temperature of the thermostat, in which the whole was immersed up to the dotted line.

The volume of air aspirated varied from three to six litres according to the temperature, and each aspiration occupied from four to twelve hours. The air bubbled through *C* at the rate of about two small bubbles per second, and always passed through at a perfectly uniform rate, although *A* was in some cases filled with powdered salt. When the experiment was finished, all the taps were closed, and the absorption apparatus detached, cleaned from lubricant by means of benzene, and weighed by Borda's method.

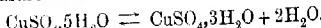
The second apparatus differed only from the first in having the U-tube, the ends of which were hermetically sealed, completely immersed, and communicating with an absorption apparatus exactly like that used with the water-bubbler. All danger of condensation on cool parts was thus avoided.

The thermostat, which was fitted with a plate glass window, was stirred by a small paddle placed to one side, and mounted on a shaft working in a bicycle hub with ball-bearings. This, when driven by an electromotor, threw a current of water upwards, and at the same time caused the whole mass to circulate. This is a method of stirring much more efficient than that in which a large paddle, covering the bottom of the thermostat, is used. A Beckmann thermometer, compared with a standard, was used, and the bath could, by means of a Lowry bulb-regulator, be kept at a temperature varying by  $0\cdot005^{\circ}$  at the most, for several days, without attention. At the higher temperatures the water was covered with a layer of cylinder oil.

Most of the water condensed in the upper part of the tube leading from the trap, and was retained by an obvious device shown in the diagram.

#### *A. Copper Sulphate Hydrate.*

The first measurements were made with the system:



Purified and recrystallised copper sulphate was used; the specimen prepared was in very small crystals, which were kept for six hours

in a press between filter paper, and then air-dried for a week. A column of 10 cm. was put in the U-tube, air aspirated through for about six hours, and the measurements begun. After the experiments, the salt was seen to have effloresced for a depth of 0·5 cm. next the air-inlet, this part being separated sharply from the rest, which was apparently unchanged.

$$\text{Temperature} = 25\cdot01^\circ. \quad \pi_{25\cdot01} = 23\cdot560 \text{ mm.}$$

$w_1$	$w_2$	$p_{25\cdot01}$ mm.
0·0075	0·0232	7·61
0·0085	0·0245	8·13*
0·0066	0·0186	8·36*
0·0065	0·0203	7·54
0·0116	0·0519	7·98
0·01924	0·0504	7·28
0·01157	0·03610	7·55
0·00949	0·02776	8·05
0·00744	0·02263	7·74

The mean (rejecting those numbers marked \*) is  $p_{25\cdot01} = 7\cdot68$  mm.

The value interpolated from Frowein's tensimetric results (*Zeitsch. physikal. Chem.*, 1887, 1, 5) is  $p_{25\cdot01} = 7\cdot35$  mm.

The dynamic pressure is thus slightly higher than the static pressure.

#### B. Barium Chloride Hydrate, $\text{BaCl}_2 \cdot 2\text{H}_2\text{O}$ .

For various reasons, it appeared desirable to use a hydrate containing less water than copper sulphate pentahydrate, and barium chloride dihydrate was next taken, purified by recrystallisation.

$$\text{Temperature } 25\cdot01^\circ.$$

$w_1$	$w_2$	$p_{25\cdot01}$ mm.
0·00690	0·03112	5·20
0·01013	0·04503	5·30
0·01390	0·04728	6·92*
0·01152	0·03766	7·20*
[25·03*]	0·01138	6·34*
0·01064	0·04222	5·26
0·01108	0·04576	5·27
	0·04952	

The mean value adopted is  $p_{25\cdot01} = 5\cdot26$  mm. Frowein's interpolated value is 5·20 mm.

Some irregularities were observed with this substance, and the experiments were not extended to higher temperatures.

#### C. Racemic Acid Hydrate, $(\text{C}_4\text{H}_6\text{O}_6 \cdot \text{H}_2\text{O})_2$ .

Kahlbaum's "pure racemic acid" was used; 100 grams were reduced to a coarse powder and placed directly into the U-tube,

(a) Temperature  $25^{\circ}\text{O}$ .  $\pi_{25} = 23.546$  mm.

(a)	$w_1$	$w_2$	$p_{25}$ mm.
0.00454		0.03854	2.77*
0.00840		0.04251	4.66*
0.01069		0.04591	5.49*
0.01672		0.03994	9.85
0.02660		0.05550	11.29
0.01701		0.04415	9.08
0.02044		0.04934	9.65
0.02196		0.04890	10.58
0.01943		0.04293	10.66
0.03004		0.06589	10.27
0.01571		0.03377	10.96
0.01409		0.03299	10.08

The mean result is  $p_{25} = 10.37$  mm.

(b) The acid, which had effloresced only near the inlet tube, was removed, well mixed, and replaced. The following numbers were obtained:

0.01095	0.03186	8.104*
0.01595	0.03667	10.24
0.01617	0.03776	10.35

(c) The acid was now removed, mixed, and distributed in three horizontal U-tubes. A current of dry air was passed over for four hours, the solid being frequently shaken so as to expose new surfaces. The whole was well mixed and recharged into the experimental tube. The results were:

0.01977	0.04416	10.51
0.01810	0.04185	10.19

(d) The acid was removed, spread out on a large porous plate, and placed in a vacuum desiccator over calcium chloride for an hour. After mixing, it was replaced by the experimental tube:

0.01090	0.02216	11.59*
0.03096	0.04623	15.77*
[24.99] 0.02142	0.05141	9.805*
0.01838	0.04104	10.55

The mean result from (a) to (d) adopted is  $p_{25} = 10.33$  mm.(e) Temperature  $20.27^{\circ}$ .  $\pi_{20.27} = 17.696$  mm.

	$w_1$	$w_2$	$p_{20.27}$ mm.
	0.00655	0.02488	4.66*
[20.29]	0.00958	0.03226	5.96
	0.01068	0.03701	4.82*
[20.295]	0.01112	0.03493	5.62*
	0.01417	0.03763	6.81
	0.02270	0.04992	8.05*
	0.01706	0.05422	5.81

Mean result adopted is  $p_{20.27} = 5.61$  mm.

(c) Temperature 29·89°.  $\pi_{29\cdot89} = 31\cdot384$  mm.

$w_1$	$w_2$	$P_{29\cdot89}$ mm.
0·01799	0·03823	14·77
0·02615	0·04761	17·16
0·01923	0·03201	18·85
0·02795	0·04620	18·98
0·03107	0·05636	17·30
0·02040	0·03423	18·70

Mean result adopted is  $p_{29\cdot89} = 18\cdot19$  mm.(d) Temperature 40·00°.  $\pi_{40} = 54\cdot97$  mm.

$w_1$	$w_2$	$P_{40}$ mm.
0·06570	0·08408	42·96
0·05295	0·06951	41·87
[40·04°]	0·01299	0·05268
0·05505	0·07144	42·36
0·01385	0·05577	43·22

Mean:  $p_{40} = 43\cdot05$  mm.(e) Temperature 50·00°.  $\pi_{50} = 92\cdot17$  mm.

$w_1$	$w_2$	$P_{50}$ mm.
0·09297	0·10784	70·49
0·08559	0·09542	82·66
0·16325	0·18573	81·02
0·03464	0·09667	80·69

Mean:  $p_{50} = 80\cdot96$  mm.*Discussion of the Results.*

The numbers for racemic acid hydrate have been represented graphically in Fig. 3. The perfect regularity of the curve shows that the pressure measured by the transpiration method is a definite magnitude, whatever interpretation may be put upon it.

The mean pressures of series (A) and (B) confirm Tammann's statement as to the higher value of the dynamic as compared with the static pressure,\* but it is believed that the results of series (C) entirely exclude any possibility of explanation by the supposed presence of saturated solution, and are in agreement with the theory indicated by the author in a previous communication (Proc., 1911, **27**, 12).

There are three possible explanations of the higher values of the dynamic pressure:

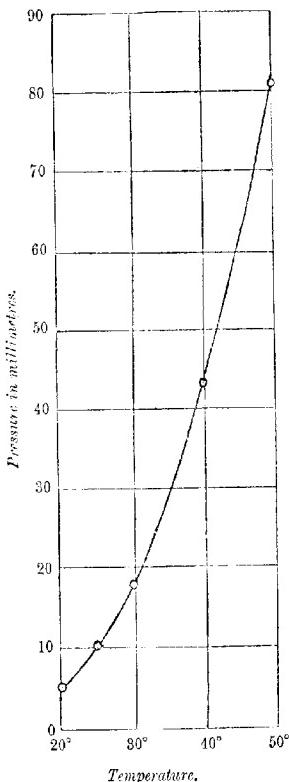
(1) That they are a consequence of incorrectness of the assumption.

\* Some further experiments with  $\text{BaCl}_2 \cdot 2\text{H}_2\text{O}$  indicate that the pressure at 25° is probably rather higher than the one recorded; the value 5·50 seems to be probable.

tion that water vapour at the pressures considered obeys the gas laws.

This explanation is excluded by Schottky's observation that the phenomenon also appears in the initial stages of a tensimetric measurement.

FIG. 3.



(2) That they are due to the presence of saturated solution retained on the crystals, or occluded in their interior.

The solution could scarcely have been occluded in the interior of the very small crystals of copper sulphate used in the experiments now described, and, if present at all, must have been adherent to the surface. If this were the case, the pressures recorded in

the first one or two experiments should always be higher than those in the later ones. Exactly the reverse is observed; the initial pressures are either very small, the pressure then rising steadily as the extent of dehydration proceeds, and finally attaining a steady value which is higher than the tensimetric pressure, or else steady all through the series. The first phenomenon is observed with series C(a), [a], C(a), [β], C(c), especially in the first, where no previous dehydration had occurred; the second is characteristic of series (A) and (B), in which the salt was dehydrated to a fairly considerable extent before beginning the measurements.

This fact, taken in connexion with another to be mentioned immediately, leaves open only the third hypothesis:

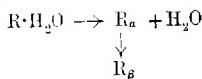
(3) That the phenomena are simply and completely explained by the initial production of an unstable, probably amorphous, lower hydrate or anhydrous salt, which passes slowly into a stable, crystalline modification.

The initial formation of such a substance is rendered probable, from an inductive point of view, by Ostwald's Principle of Successive Reactions, and is apparently also in agreement with the representation of the process of dehydration which is given by the molecular theory. The vapour pressure of a pure liquid is the same whether determined statically or dynamically. The necessary conditions for this are obviously that the surface of separation of the two phases remains unaltered in character when either phase is increased at the expense of the other, and that the readjustment of temperature in the liquid can, by conduction of heat to it from the surroundings, occur sufficiently rapidly. In the case of a pair of isotropic phases (for example, pure liquid and vapour), these can be fulfilled, because the equilibrium is attained and maintained by the statistical equality in the numbers of molecules leaping out of, and returning to, the liquid in any interval of time. By reason of the wholly unco-ordinated molecular motion in each phase, the transference of a finite amount of one phase to the other can produce no effect on the losing phase, which could not have been produced by withdrawing a portion of the phase in bulk, which, of course, has no influence on the equilibrium. If, however, one of the phases is a crystalline solid, this is not necessarily the case. In a crystal of a hydrated salt, one may suppose that the molecular aggregates of anhydrous salt and attached water are oscillating in small excursions about fixed points which are arranged in definite space-lattices ("Raumgittern"), determining the crystalline form. If the kinetic energy of one of these aggregates exceeds a certain finite amount, the component molecules part company, and the molecules of water are ejected forcibly from the space-lattice. This

will produce a disruption of that portion of the lattice adjacent to the centre of disturbance; it breaks down, and the molecules of solid lower hydrate, or anhydrous salt, remaining behind fall together into an amorphous aggregate which only slowly rearranges itself into a new space-lattice, and so gives rise to a stable, crystalline form. The molecules of water, which now form an isotropic vapour phase, can obviously not return to their original positions in the first space-lattice, and a condition of mobile equilibrium, exactly analogous to that existing between a liquid and its vapour, is excluded by the nature of the system (compare Schenck, *Centr. Min.*, 1900, p. 313, who finds that the dissociation pressure is different over different crystal-faces).

The molecular theory of dehydration of a crystalline hydrate has, along with other dissociation phenomena in heterogeneous systems of similar character, offered difficulties which do not appear to be completely overcome even at present. The case under discussion may, however, be considered from another point of view, which, whilst it does not enable us to see all that is going on during the process, is at least in agreement with the observed phenomena.

If we regard racemic acid hydrate for simplicity as  $C_4H_6O_6 \cdot H_2O$ , or  $R \cdot H_2O$ , we can represent the process of dehydration as follows:



in which  $R_a$  is the unstable form first produced, which passes slowly into the stable, crystalline form,  $R_b$ .

The dissociation pressure of water vapour over such a system will be a function, not only of the temperature, but also of the absolute and relative amounts of  $R_a$ ,  $R_b$  present; it will, for example, be zero over a perfectly unefloresced crystal, when:

$$R_a = R_b = 0.$$

The removal of water doubtless occurs at a definite number of centres of efflorescence which are distributed throughout the salt. These spread through the mass, and a limited region of efflorescence is formed in the vicinity of the air inlet-tube. The extent of this region will depend on the facility with which dehydration occurs, and on the number of pre-formed nuclei. It was found, for example, that a much longer column of barium chloride hydrate was required to attain saturation than of copper sulphate hydrate, although the dissociation pressures are not greatly different. The initial period of small vapour pressure therefore corresponds with the formation of an efflorescence region. When such a region is formed, the process of dehydration is confined to that part of the

system. Now the first product of dehydration will be the unstable lower hydrate, and when sufficient of this has accumulated, the pressure attains saturation. All the time, however, this hydrate is passing over into its stable crystalline form, in contact with which the vapour exists at a smaller pressure. There will obviously be a time when the amounts of  $R_a$  and  $R_b$  are so adjusted that the pressure attains a maximum. Further dehydration leads to a falling, but ultimately steady, pressure, because the latter is now determined principally by the large surface of  $R_b$ , in comparison with which the newly-formed  $R_a$  is negligible. The presence of the  $R_a$  shows itself, however, in the somewhat larger value of the steady dynamic pressure as compared with the static or tensimetric pressure, where the system has been left for a time which allows the whole of the  $R_a$  to pass into stable  $R_b$ .

The strict mathematical treatment of the system, which resembles that of motion in some dynamical systems, is without interest in this case, on account of the complications introduced by the experimental method; the results could show nothing beyond what has just been stated, and the discussion is omitted here. It may be observed, however, that a treatment of somewhat simpler systems than the present, such as occur, for example, in the "ageing" of deposited catalytic surfaces, would present points of interest, and this will probably form the subject of a later communication.

Measurements of the tensimetric pressure of racemic acid hydrate, and of some thermal magnitudes, are also in progress, with a view to comparison of the results with Nernst's new theory.

#### *Summary.*

(1) A method of measuring the pressure of water vapour in contact with a salt hydrate has been elaborated. The weight of water lost by the hydrate in a current of air is compared with that lost by pure water, in a special apparatus.

(2) The results with copper sulphate pentahydrate, barium chloride dihydrate, and racemic acid hydrate show that the initial pressures are very small, but with increasing dehydration the pressure rises, attains a maximum, and then falls to a steady value which is slightly higher than the value obtained by tensimetric (static) methods.

(3) These results are shown to be in accordance with the view that the first product of dehydration is an unstable, probably amorphous, lower hydrate or anhydrous salt, which slowly passes into a stable, crystalline form. They exclude the explanation suggested by Tammann that the somewhat higher value of the

dynamic pressure is due to saturated solution adsorbed on the solid salt.

In conclusion, I desire to thank Dr. Lapworth for the interest he has shown during the course of the work.

CHEMICAL DEPARTMENT,  
UNIVERSITY OF MANCHESTER.

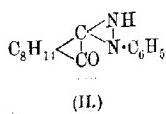
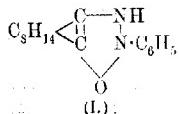
**LVIII.—Studies in the Camphane Series. Part XXIX.  
A New Phenylhydrazone of Camphorquinone.**

By MARTIN ONSLOW FORSTER and ADOLF ZIMMERLI.

CAMPHORQUINONEPHENYLHYDRAZONE was first described by Claisen and Bishop (*Sitzungsber. K. Bayer. Akad.*, 1890, 460, 478). They prepared it from hydroxymethylene camphor and benzene diazonium chloride, whilst Claisen and Manasse (*Annalen*, 1893, **274**, 87) utilised it in their characterisation of camphorquinone, which they subjected to condensation with phenylhydrazine. Betti (*Ber.*, 1899, **32**, 1995), who produced it by the action of benzenediazonium chloride on sodium camphorcarboxylate, claimed to recognise an enolic form of the substance, answering to the ferric chloride test and melting at  $180^\circ$ , in addition to a ketonic form which melted at  $155^\circ$  and did not develop colour with ferric chloride, whilst a third material, giving colour with ferric chloride, melted at  $165^\circ$ , and was regarded by Betti as a "keto-enolmisch-form." Lapworth and Hann, who were the first to draw attention to the mutarotation displayed by solutions of the phenylhydrazone (Trans., 1902, **81**, 1514), threw doubt on the separate existence of any but the substance of highest melting point, agreeing, however, with Betti's conclusion that it probably represents the pure enolic

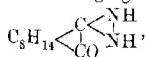
form,  $\text{C}_8\text{H}_{14}\begin{array}{c} \text{C}=\text{N}\cdot\text{C}_6\text{H}_5 \\ || \\ \text{C}-\text{OH} \end{array}$ , which undergoes incomplete trans-

formation into a ketonic modification when dissolved, as indicated by the alteration in optical activity. These views were not accepted by Armstrong and Robertson (Trans., 1905, **87**, 1272), who suggested that the derivative of high melting point is to be represented by the formula (I), and that on dissolution in benzene



it is changed, to the extent of about 10 per cent., into the isomeric substance (II). The last-named investigators, however, did not adduce any chemical evidence for their conclusions, which were based on convictions as to relation between structure and such optical properties as colour and rotatory power. Two years later, Baly, Tuck, Marsden, and Gazdar were led from a study of absorption spectra to regard the phenylhydrazone and *p*-bromo-phenylhydrazone of camphorquinone as having the conventional ketonic formula in neutral solutions, recognising a modification of this structure in presence of sodium ethoxide (Trans., 1907, **91**, 1572); they were not able to find any spectrochemical support for difference in type of structure between the diphenylhydrazone and other condensation products of camphorquinone, such as Armstrong and Robertson believed they had brought to light. A few months ago Auwers recorded attempts to recognise an isomeric form of the phenylhydrazone; these led consistently to the isolation of one modification only, "die alle Kennzeichen einer einheitlichen Substanz aufwies" (Annalen, 1910, **378**, 245), and regarded by the author as a conventional phenylhydrazone.

We have recently described experiments dealing with the action of hydrazine, semicarbazide, and phenylcarbamylhydrazide on camphorquinone, which, in our opinion, point to the existence of stereoisomerism among the products, similar in nature to that prevailing among oximes as represented by the Hantzsch-Werner hypothesis (Trans., 1910, **97**, 2156). The conclusion was based on the discovery of two isomeric hydrazones, which were not only directly convertible into diazocamphor by oxidation, but which also arose from that substance by mild reduction. The absence of any grounds, stereochemical or otherwise, for representing the hydrazine residue in these derivatives as belonging to the cyclic type:



seemed to point unmistakably to stereoisomerism of the above-mentioned character, and to stamp these isomeric substances as conventional hydrazones with azethenoid linking. In these circumstances, it appeared to us possible that a more careful search for the missing phenylhydrazone would bring this substance to light, and would show that it is allied to the existing compound by a relationship similar to that which connects the two hydrazones. This inquiry has resulted in the isolation of such an isomeride, which we propose to call the  $\beta$ -phenylhydrazone, referring to the better known derivative as the  $\alpha$ -phenylhydrazone.

*Camphorquinone- $\beta$ -phenylhydrazone* is a bright yellow, crystalline substance, melting at  $36^\circ$ , and having  $[\alpha]_D 375^\circ$  in an alcoholic solu-

tion of 1 per cent. It is very much more freely soluble than the  $\alpha$ -modification, and is slightly volatile in steam. It is produced in association with the less fusible compound when camphorquinone undergoes condensation with phenylhydrazine, but as the equilibrium is being continually disturbed by the separation of sparingly soluble solid, the proportion obtained in this way is very small. A more convenient source is the  $\alpha$ -phenylhydrazone itself, which yields about 90 per cent. when the temperature of the fused substance is raised to  $210^\circ$ , the  $\beta$ -phenylhydrazone being separated from the resulting mixture by distillation in steam or by extraction with a small proportion of cold petroleum. When heated, either alone or in alcoholic solution, it is transformed into an equilibrium mixture with the  $\alpha$ -modification; by following this change in the polarimeter, it is possible to show that the same proportion of the two isomerides constitutes this mixture, whether the material originally dissolved is the  $\alpha$ - or the  $\beta$ -modification.

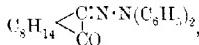
Thus, in all respects, the new phenylhydrazone fits into the gap in the series of condensation products from camphorquinone and hydrazine, semicarbazide, phenylcarbamylhydrazide, and phenylhydrazine, as shown in the following table:

Derivative.	$\alpha$ -Series.		$\beta$ -Series.	
	M. p.	[ $\alpha$ ] <sub>D</sub>	M. p.	[ $\alpha$ ] <sub>D</sub>
Hydrazone.....	206 <sup>o</sup>	27 <sup>o</sup>	102 <sup>o</sup>	231 <sup>o</sup>
Acetylhydrazone .....	239	265	150	224
Semicarbazone .....	236	278	147	201
Phenylcarbamylhydrazone .....	211	229	161	192
Phenylhydrazone .....	190	431	36	375

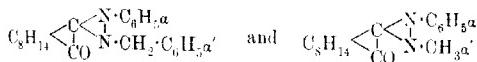
The regularity in declension of melting point and specific rotatory power on passing from the  $\alpha$ - to the  $\beta$ -series is so marked as to suggest that the relationship which connects the members of a pair is the same in each case, and thus the argument for regarding the two phenylhydrazones as stereoisomeric seems a strong one, provided this view of the hydrazones themselves can be accepted. There is one point, however, in which the phenylhydrazones differ from their prototypes. Whilst these of the  $\alpha$ -series are colourless in distinction from the pale yellow colour of their  $\beta$ -modifications, the  $\alpha$ -phenylhydrazone has approximately the same tint as the  $\beta$ -hydrazone, and the  $\beta$ -phenylhydrazone is bright yellow. We are aware that Armstrong and Robertson believe the  $\alpha$ -phenylhydrazone to be colourless, but they are the only chemists who have made this claim, and it is by no means clear that they ever produced it in this condition, the nearest recorded approach being a specimen described by Robertson (Trans., 1905, 87, 1298) as "all but white" under benzene, becoming "very pale yellow" on drying. It does not seem to us improbable, however, that the  $\alpha$ -phenylhydrazone

should be faintly coloured, even though the parent hydrazone is colourless, as the effect might be reasonably expected from the phenyl group, which undoubtedly exerts an auxochromic influence when replacing hydrogen in the  $\beta$ -hydrazone.

To the arguments brought against possible differences in structure between members of the two series, we have nothing to add to our previous communication, excepting that there is not the slightest ground for regarding the  $\beta$ -phenylhydrazone as an enolic form of the less soluble modification; moreover, this opening seems to have been effectually closed by Baly, Tuck, Marsden, and Gazdar. Furthermore, it is no longer proper to speak of stable and labile forms of camphorquinonephenylhydrazone; both are stable in the solid phase, both are labile when dissolved. It is necessary, also, to correct a misconception as to the mutarotation of the  $\alpha$ -phenylhydrazone in alcohol, which Lapworth and Hann regarded as taking place so rapidly that the specific rotatory power reaches its final value before an observation can be made. As a consequence of our experiments, it appears more probable that at this stage the mutarotation has not begun, because the rotatory power is rapidly diminished on heating, and arrives finally at a point approximately the same as that to which the rotatory power of the  $\beta$ -phenylhydrazone may be raised by similar treatment. Another misunderstanding, embodied in Robertson's conclusion that "the labile form has practically no rotatory power," is also removed, and carries with it whatever support that deduction may be regarded as giving to the views of Armstrong and Robertson concerning the constitution of the condensation products of camphorquinone. It appears to us, in fact, that the whole case for regarding camphorquinonephenylhydrazone as structurally abnormal is undermined. The basis of the argument was the low molecular rotatory power ( $120^\circ$ ) of the diphenylhydrazone,



when compared with those ( $2200^\circ$  and  $2430^\circ$ ) of the phenylbenzylhydrazone and phenylmethylhydrazone, represented by Armstrong and Robertson as:



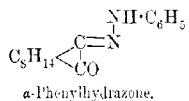
respectively, coupled with the deep yellow colour of the first-named substance as compared with the "colourless" and "almost colourless" appearance of the others. The intermediate molecular rotatory power ( $850^\circ$ ) of the phenylhydrazone, which they also describe as colourless, led them to represent it by a third type of

formula,  $C_8H_{14}\begin{array}{c} \text{C}-\text{NH} \\ \diagdown \quad \diagup \\ \text{C}=\text{N} : \text{C}_6\text{H}_5 \\ | \\ \text{O} \end{array}$ , and believing that in benzene

solution about one-tenth of this substance is converted into "a metameride having little, if any, optical activity," they regard this hypothetical product as being similar in type to the phenylbenzylhydrazone and phenylmethylhydrazone, but in order to explain the supposed absence of optical activity, they place the

phenyl group in the alternative position,  $C_8H_{14}\begin{array}{c} \text{C}-\text{NH}_2 \\ \diagup \quad \diagdown \\ \text{CO} \quad \text{N} : \text{C}_6\text{H}_5 \end{array}$ .

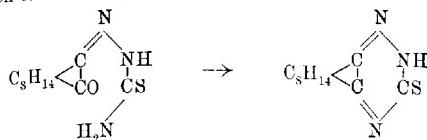
It is difficult to take these speculations seriously, since not one shred of chemical evidence has been brought forward in support of them, and they appear to us especially untrustworthy now that the substance which Armstrong and Robertson, without having isolated it, described as colourless and inactive, proves, when isolated, to be bright yellow and possessed of specific molecular rotation  $948^\circ$  in benzene solution. The scheme adopted in dealing with the hydrazones, semicarbazones, and phenylcarbamylhydrazones, on the other hand, would classify the  $\alpha$ - and  $\beta$ -phenylhydrazones as *anti*- and *syn*-carbonylic respectively:



and the comparatively strong colour of the  $\beta$ -phenylhydrazone would then find its explanation in the concentration of unsaturated atoms prevailing in the *syn*-configuration.

Concurrently with these experiments, we have studied the thiosemicarbazone and phenylthiocarbamylhydrazone of camphorquinone, and find that it is not possible in either case to isolate more than one modification. When condensation takes place between the diketone and thiosemicarbazide, the  $\alpha$ - and  $\beta$ -modifications are certainly produced, but the facility with which the latter is transformed into the thiotriazine by loss of water precludes its isolation; thus the case of the thiosemicarbazones resembles that of the benzylsemicarbazones, of which one modification only is known, the substance supposed originally to be the isomeride having been shown by Blitz and Arndt (*Ber.*, 1902, **35**, 344) to consist of the diphenyloxytriazine. The properties of the  $\alpha$ -thiosemicarbazone, which dissolves in alkali without undergoing change, agree with what might be expected from the replacement of oxygen by sulphur in the  $\alpha$ -semicarbazone.

As regards the thiotriazine produced by the intramolecular condensation of the  $\beta$ -thiosemicarbazone,

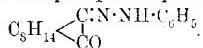


there is reason to believe that the foregoing representation is less applicable to the sulphur compound than is the corresponding formula to the oxytriazine. The behaviour of the silver salt, which loses silver sulphide by the action of boiling water, seems to indicate the alternative expression for the thiotriazine, that, namely, containing the  $\text{N}(\text{C}\cdot\text{SH})$  group. Some difference in type of structure between the oxytriazine and the thiotriazine would appear also to be indicated by the fact that, whilst the exchange of oxygen for sulphur in the semicarbazone and phenylcarbamylhydrazone is attended with elevation of specific rotatory power, amounting to  $38^\circ$  and  $30^\circ$  respectively, the thiotriazine has  $[\alpha]_D -73.3^\circ$ , as compared with  $[\alpha]_D 22.6^\circ$  observed for the oxytriazine.

The expectation that the action of phenylthiocarbimide on the  $\alpha$ - and  $\beta$ -hydrazone would lead to phenylthiocarbamylhydrazones corresponding with the phenylcarbamylhydrazones described in our previous communication has not been fulfilled, the product from both hydrazones being the same.

#### EXPERIMENTAL.

*The Isomeric Camphorquinonophenylhydrazones,*



In order to avoid the possibility of transformation being effected by the acetic acid which is free in the usual method of producing phenylhydrazones, the diketone and the base were allowed to undergo condensation in ethereal solution. The phenylhydrazine was first purified by Fischer's method, namely, crystallisation from chilled ether, which yields it in the form of a grey, silvery powder, remaining dry at temperatures below  $20^\circ$ . About 60 grams of camphorquinone were dissolved in 250 c.c. of warm ether, to which was added the calculated amount of phenylhydrazine diluted with 50 c.c. of the solvent. The action which immediately set in was moderated by cooling, and after an interval of sixteen hours the hard, crystalline mass was collected, and the mother liquor allowed to evaporate without being heated, depositing a further crop of crystals embedded in a deep yellow oil. In our earlier experiments,

the oil was submitted to distillation in steam, because this treatment was found to separate the  $\beta$ -phenylhydrazone effectively from its less volatile isomeride, but the process is a tedious one, about twelve hours being occupied by the passage of 5 grams. In consequence of this, later procedure consisted in extracting the residue with small quantities of cold petroleum, which leaves most of the  $\alpha$ -phenylhydrazone undissolved, and, on evaporation, yields the  $\beta$ -phenylhydrazone as a yellow, viscous mass containing a small proportion of the isomeride. The quantities of crude materials obtained in this fashion correspond with 85 per cent. of the  $\alpha$ -compound, and 10 per cent. of the isomeric substance.

Purification of the  $\alpha$ -phenylhydrazone was effected by rapid successive crystallisations from hot benzene or alcohol, and trouble has been taken to procure a colourless specimen; this, however, could not be accomplished, even by working throughout in artificial light. Animal charcoal has no influence on the colour of good specimens, and the device employed for decolorising benzenediazophenylsemicarbazinocamphor (Trans., 1906, **89**, 229), namely, addition of zinc dust to a cold solution in glacial acetic acid, was without influence on the colour of the solution. It is our opinion therefore that camphorquinone  $\alpha$ -phenylhydrazone is coloured, and in its palest forms, derived by precipitation with water from an alcoholic solution, the shade of yellow is faintly green, very similar, in fact, to that of camphorquinone- $\beta$ -hydrazone described in our paper already quoted. It should be noted, however, that the appearance of the  $\alpha$ -phenylhydrazone depends largely on the compactness of the mass observed; thus crystals which have separated from a solution in petroleum appear less coloured than those from alcohol until withdrawn from the liquid, because the amount dissolved is very small, and the deposit is comparatively bulky.

The want of agreement between the melting points recorded by various chemists who have worked with this substance is explained by the facility with which transformation into the more fusible isomeride takes place. The temperatures are, in chronological order, 170—171° (Claisen and Manasse), 180° (Betti), 180—181° (Lapworth and Hann), 180° (Robertson), and 178—180°, occasionally 183° (Auwers). Some years ago, a specimen obtained by one of us as a by-product of the interaction of  $\alpha\alpha$ -bromonitrocamphe and phenylhydrazine (Trans., 1902, **81**, 869) was stated to melt at any temperature between 183° and 190° according to the rate of heating, and this observation we are able to confirm; if the substance is not absolutely dry, or if the temperature is raised very slowly, the conversion into the  $\beta$ -phenylhydrazone makes sufficient headway to furnish, locally, a solvent for the less fusible form,<sup>20</sup>

that under these conditions one is taking the melting point of the  $\alpha$ -compound mixed with its solution in the  $\beta$ -modification. If the purified  $\alpha$ -phenylhydrazone is plunged into a bath at 175—180°, the temperature may be raised slowly to 190° before fusion is complete.

The specific rotatory power of our specimen in absolute alcohol was somewhat lower than that recorded by Lapworth, being  $[\alpha]_D 431^\circ$  in 1 per cent. solution (by volume); the corresponding figures for pyridine and nitrobenzene were 435.5° and 458.9° respectively.

*Camphorquinone  $\beta$ -phenylhydrazone.*—Suggested by the relative volatility of the isomeric camphorquinonehydrazones, our first attempts to prepare the missing  $\beta$ -phenylhydrazone consisted in heating the  $\alpha$ -phenylhydrazone at its melting point during several minutes, and then passing a current of steam through the gummy product, when there slowly distilled a yellow oil which was extracted with ether and, after drying, allowed to remain in the vacuum desiccator until solid. More convenient procedure, however, consists in heating the  $\alpha$ -phenylhydrazone in quantities of about 10 grams until all has melted, and the temperature of the bath has reached 210°, when the cooled product is extracted with a small quantity of light petroleum, filtered from about 8 per cent. of the  $\alpha$ -phenylhydrazone, and the solvent evaporated without being heated. On stirring the viscous residue, it solidifies very rapidly, especially if sown with a few crystals of the substance. The hard, crystalline phenylhydrazone melts at 36°, and has been crystallised from chilled light petroleum or from diluted alcohol without undergoing alteration of melting point or of optical activity.

0.4510 gave 1.2361 CO<sub>2</sub> and 0.3187 H<sub>2</sub>O. C = 74.75; H = 7.91.

0.2375 " 22.4 c.c. N<sub>2</sub> at 18° and 757 mm. N = 10.93.

C<sub>20</sub>H<sub>20</sub>ON<sub>2</sub> requires C = 75.00; H = 7.81; N = 10.93 per cent.

The most convenient way to purify the new phenylhydrazone is to dissolve 10 grams in about 100 c.c. of alcohol, add 15 c.c. of water, and then cool the solution to the neighbourhood of -15°, when vigorous stirring brings about the separation of half the material in minute, yellow crystals; by slow separation from the mother liquor, these take the form of lustrous, transparent, six-sided plates. The colour of the dry substance is much deeper than that of the  $\alpha$ -phenylhydrazone, approximating more to that of camphorquinone itself; its solubility is very much greater, 10 grams being dissolved readily by 5 grams of petroleum (b. p. 40—50°), or by 10 c.c. of cold absolute alcohol. Solutions of the  $\beta$ -phenylhydrazone are much brighter yellow than those of the isomeride except in the case of nitrobenzene, where this comparison is inverted.

The melting point is not depressed by admixture with the  $\alpha$ -phenylhydrazone, and if equal quantities of the two substances are used, the temperature may be raised to about  $170^\circ$  before fusion is complete; in this respect therefore the behaviour of the two phenylhydrazones resembles that of the hydrazones and their other derivatives, and also that of the two modifications of *isomeric* camphor.

The specific rotatory power of the  $\beta$ -phenylhydrazone when dissolved in alcohol has been determined with many different specimens, prepared both by distillation in steam and by extraction with petroleum; the uniformity of this constant at  $[\alpha]_D\ 375^\circ$  for a 1 per cent. solution (by volume) establishes the individuality of the new isomeride. In benzene, pyridine, and nitrobenzene, the respective constants are  $369.5^\circ$ ,  $395.5^\circ$ , and  $420.5^\circ$ . Addition of ethereal ferric chloride to solutions of the phenylhydrazones does not give the least justification for regarding either as an enolic modification of the other.

#### *Interconversion of the Isomeric Phenylhydrazones.*

As already stated, the  $\alpha$ -phenylhydrazone is rapidly converted into the  $\beta$ -modification when fused; the converse change is brought about by carrying the temperature of liquefied  $\beta$ -phenylhydrazone to the melting point of the less fusible form, and the proportion of isomerides in the resulting mixture is independent of the identity of the initial material. The composition of the mixture depends on the temperature at which the transformation is effected, and the foregoing conditions, being more favourable to the existence of the  $\beta$ -modification, do not illustrate in the most satisfactory manner the conversion of this form into the  $\alpha$ -isomeride, the percentage of which does not exceed 10 per cent. If alcoholic solutions of the two phenylhydrazones are separately boiled under reflux during five hours, however, the proportion of the  $\alpha$ -derivative in the resulting equilibrium mixture is raised to nearly 40 per cent., which, in view of the sparing solubility of the material, may be recognised without difficulty.

In order to place the interconversion of the isomeric phenylhydrazones upon a quantitative basis, a series of polarimetric observations has been made with solutions containing one gram of each modification in 100 c.c. of absolute alcohol, these being separately heated at  $63^\circ$  during a period of twelve hours. The initial rotation having been recorded, each solution was distributed among a number of similar tubes; these were withdrawn at suitable intervals and cooled to the original temperature ( $16^\circ$ ) as rapidly as possible, the contents being transferred to the instrument in a

3-cm. tube without delay. The following readings were thus obtained:

Time in Minutes.	$\alpha$ -Phenylhydrazone.			$\beta$ -Phenylhydrazone.		
	$\alpha_0$ .	Weight transformed.	$k_1 + k_2$ .	$\alpha_0$ .	Weight transformed.	$k_1 + k_2$ .
9	12°58'	—	—	11°15'	—	—
30	12 46	0·0990	0·0026	11 20·5	0·0544	0·0021
60	12 37·5	0·1832	0·0027	11 25·5	0·1040	0·0021
90	12 29	0·2674	0·0029	11 29·5	0·1435	0·0021
120	12 23	0·3268	0·0029	11 33	0·1782	0·0021
180	12 15	0·4060	0·0023	11 40	0·2475	0·0023
360	12 3	0·5218	0·0026	11 50	0·3465	0·0023
480	11 59·5	0·5590	0·0026	11 51·5	0·3614	0·0020
720	11 57	0·5851	0·0025	11 55	0·3961	0·0022
$\infty$	11 56	0·5940	—	11 56	0·4060	—
	Mean.....	0·0027		Mean.....	0·00215	

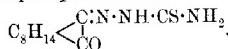
In the foregoing table the figures recorded in the columns headed  $k_1 + k_2$  are calculated from the equation:

$$k_1 + k_2 = \frac{1}{t} \log \frac{x_0 - x_\infty}{x_t - x_\infty},$$

where  $k_1$  and  $k_2$  are the velocity-constants of the isomeric change in the two directions, and  $x_0$ ,  $x_\infty$ , and  $x_t$  are the observed rotations initially, finally, and at time  $t$  respectively. This is the relation employed by Küster, Trey, Lowry, Hudson, Tubandt, and others in dealing with problems of similar character, and it will be noticed that whilst the values for  $k_1 + k_2$  agree among themselves for the same phenylhydrazone, they are not identical for the two phenylhydrazones. Although this disagreement should not occur, other workers have encountered the same peculiarity, sometimes in a more pronounced form, and it is probably due to some disturbing influence affecting the first few observations; this view is confirmed by calculations based on the later readings only, when  $k_1 + k_2$  is nearly the same for both directions.

These results are embodied in the curves on p. 488.

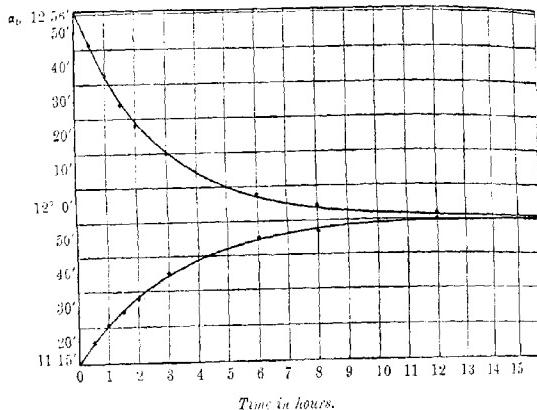
#### The Camphorquinonethiosemicarbazones,



Thiosemicarbazide dissolved in 5 parts of boiling water was added to one molecular proportion of camphorquinone in 3 parts of hot acetic acid, when the yellow colour disappeared, action being complete after fifteen minutes under reflux; diluting the cold liquid with water precipitated an oil which rapidly crystallised, the yield being 95 per cent. of that required by theory. On recrystallisation from water or carbon disulphide, the appearance of pale yellow prisms, having ill-defined faces, and melting indefinitely at

122—137°, suggested the occurrence of mixed crystals containing both forms, and this was confirmed by the failure of repeated crystallisation from other solvents, such as benzene, ethyl acetate, chloroform, and glacial acetic acid, to yield a definite product. On dissolving the crystals in alcohol, however, and scratching the sides of the vessel, there separated the  $\alpha$ -thiosemicarbazone in colourless, lustrous crystals, containing 1 mol.  $C_2H_6O$ , and the same material arose on evaporating the mother liquor on the water-bath or in the vacuum desiccator, so that the  $\beta$ -thiosemicarbazone could not be isolated:

0·4968 lost 0·0794 during half an hour at 120°. Loss = 15·98.  
 $C_{11}H_{17}ON_3S + C_2H_6O$  requires  $C_2H_6O = 16\cdot14$  per cent.



Interconversion of the camphorquinonephenylhydrazones: 1 per cent. solution,  
 3-dm. tube.

Upper curve:  $\alpha$ -Phenylhydrazone. Lower curve:  $\beta$ -Phenylhydrazone.

The substance, when free from alcohol, is very pale greenish-yellow, and melts at 174°:

0·1290 gave 19·8 c.c.  $N_2$  at 19° and 757 mm.  $N = 17\cdot36$ .

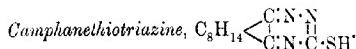
0·2679 „ 0·2593  $BaSO_4$ .  $S = 13\cdot29$ .

$C_{11}H_{17}ON_3S$  requires  $N = 17\cdot57$ ;  $S = 13\cdot39$  per cent.

Camphorquinone- $\alpha$ -thiosemicarbazone is readily soluble in warm alcohol, benzene, or chloroform, but is insoluble in petroleum. Alkali hydroxides readily form orange-yellow solutions, from which carbon dioxide precipitates the substance unchanged, but it dissolves also in hot sodium carbonate, and crystallises as the liquid cools;

continued heating of a solution in alkali hydroxide gives rise to camphor. A 1 per cent. solution (by volume) in chloroform gave  $\alpha_D -9^{\circ}26'$  in a 3-dcm. tube, whence  $[\alpha]_D 314^{\circ}4$ .

Transformation of the  $\alpha$ -thiosemicarbazone into the  $\beta$ -modification takes place when the substance is heated at the melting point, being followed by removal of water and consequent production of the thiotriazine; it has not been possible therefore to produce the  $\beta$ -thiosemicarbazone by the process which was applied to the  $\beta$ -phenylhydrazone. Nor could the second isomeride be separated by alkalies, as in the case of semicarbazones themselves, because when a mixture of the  $\alpha$ - and  $\beta$ -thiosemicarbazones is treated with these agents, the  $\beta$ -modification is transformed so rapidly into the thiotriazine that there is no opportunity to separate it from the  $\alpha$ -isomeride, which, however, is not convertible into the thiotriazine.



The most convenient source of the thiotriazine is the crude product of condensation between camphorquinone and thiosemicarbazide, which contains approximately 50 per cent. of the  $\beta$ -thiosemicarbazone; on dissolving this mixture in alkali hydroxide and saturating the solution with carbon dioxide, the  $\alpha$ -thiosemicarbazone is precipitated, whilst the filtrate yields the thiotriazine on acidification with dilute hydrochloric acid. When recrystallised from alcohol, it forms fern-like aggregates of lustrous, yellow prisms, melting at  $207^{\circ}$ :

$0.1673$  gave  $0.1763$   $\text{BaSO}_4$ .  $S = 14.46$ .

$\text{C}_{11}\text{H}_{15}\text{N}_3\text{S}$  requires  $S = 14.47$  per cent.

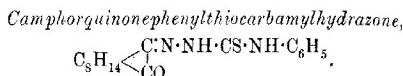
The thiotriazine dissolves readily in hot methyl and ethyl alcohols, benzene, chloroform, pyridine, or ether, but only sparingly in hot petroleum or water; it is soluble in alkali hydroxides, alkali carbonates, and ammonia, but is insoluble in dilute acids. A 1 per cent. solution (by volume) in chloroform gave  $\alpha_D -2^{\circ}12'$  in the 3-dm. tube, whence  $[\alpha]_D -73.3$ .

Derivatives of the thiotriazine with heavy metals are produced very easily. Mercuric chloride gives a voluminous, white precipitate, which dissolves in hot water, and separates in slender, colourless needles on cooling; silver nitrate and copper acetate give pale yellow and green precipitates respectively.

*Conversion into Camphaneoxytriazine.*—An attempt to replace sulphur by heating the thiotriazine with water and mercuric oxide was unsuccessful; the yellow colour disappeared, but the filtered liquid deposited crystals of the above-mentioned mercury salt. On adding a solution of ammoniacal silver oxide which contained only

just sufficient ammonia to a solution of the thiotriazine (1 gram) in hot water (200 c.c.), however, the pale yellow silver derivative gradually became dark on further heating, and ultimately changed into a black, granular mass of silver sulphide; after four hours under reflux, the filtered liquid was saturated with sodium chloride and extracted with ether, which deposited the oxytriazine.

The acetyl derivative of the oxytriazine was obtained from the thiotriazine by heating it with acetic anhydride under reflux during one hour.



The same derivative was obtained alike by heating the  $\alpha$ -hydrazone with the calculated amount of phenylthiocarbimide in alcohol under reflux during three hours, and by action of the thiocarbimide on the  $\beta$ -hydrazone in benzene during twenty-four hours at the laboratory temperature. Recrystallisation from hot benzene gave small, lustrous, pale yellow leaflets, melting at 184°:

0·0988 gave 11·5 c.c. N<sub>2</sub> at 18° and 764 mm. N=13·52.

0·2916 " 0·2134 BaSO<sub>4</sub>. S=10·05.

$\text{C}_{11}\text{H}_{12}\text{ON}_3\text{S}$  requires N=13·39; S=10·16 per cent.

The substance dissolves somewhat readily in hot alcohol, benzene, chloroform, or ethyl acetate, but is insoluble in petroleum; a solution in hot sodium hydroxide is deep yellow. The 1 per cent. solution (by volume) in chloroform gave  $\alpha_D^{25}$  7°47' in the 3-cm. tube, whence  $[\alpha]_D$  259·4°. An attempt to produce it by heating camphorquinone-thiocsemicarbazone with aniline was not successful.

ROYAL COLLEGE OF SCIENCE, LONDON.  
SOUTH KENSINGTON, S.W.

#### LIX.—*The Constituents of Withania somnifera.*

By FREDERICK BELDING POWER and ARTHUR HENRY SALWAY.

THE plant *Withania somnifera*, Dunal (Nat. ord. Solanaceae), occurs in South Africa, where it is found in gardens and waste places, and is known under the Kaffir name of *ubu-Yumba*. It is also a native of the west coast of India, and is said to be common along the shores of the Mediterranean. The plant is described in De Candolle's *Prodromus*, Vol. 13, Part I, p. 453, and has been recorded by

J. Medley Wood in a List of the Flora of Natal (*Trans. South African Phil. Soc.*, 1908, **18**, Part II, 197), while a more extended description of its characters and uses is given in Smith's "Contribution to South African Materia Medica," pp. 145, 166, and in the "Pharmacographia Indica," Vol. II, p. 566. Although various medicinal properties have been attributed to the plant, it is particularly stated to act as a sedative and hypnotic (*Amer. J. Pharm.*, 1891, **63**, 77), and this action has been considered by Trebut (*The Lancet*, 1886, **1**, 467) to be due to the presence of an alkaloid, which was provisionally designated by him "somniferine." Inasmuch as nothing of a definite nature has been recorded respecting this alkaloid or the other constituents of the plant, it seemed desirable to subject it to a more complete examination, and the results are summarised at the end of this paper.

#### EXPERIMENTAL.

The material used for the present investigation was received directly from South Africa, and consisted of both the root and the overground portion of the plant.

##### I. Examination of the Root.

A small portion of the root was tested for the presence of an alkaloid, with a positive result.

Fifty grams of the ground material were subsequently extracted in a Soxhlet apparatus with various solvents, when the following amounts of extract, dried at 100°, were obtained:

Petroleum (b. p. 35—40)	extracted	0·22 gram	= 0·44 per cent.
Ether	"	0·35 "	= 0·70 "
Chloroform	"	0·23 "	= 0·46 "
Ethyl acetate	"	0·35 "	= 0·70 "
Alcohol	"	2·15 "	= 4·30 "
		Total.....	3·30 grams or 6·60 per cent.

For the purpose of a complete examination, 18·37 kilograms of the ground root were extracted by continuous percolation with hot alcohol. After the removal of the greater portion of the alcohol, there remained a dark-coloured, viscid extract, which amounted to 2·7 kilograms.

##### Distillation of the Extract with Steam: Separation of an Essential Oil.

The whole of the above extract was mixed with water, and the mixture distilled in a current of steam for several hours. The distillate, which contained a small amount of an essential oil, was

shaken with ether, the ethereal liquid being washed, dried, and the solvent removed. The essential oil thus obtained possessed a light brown colour, a pungent odour, and amounted to 1·2 grams, being thus equivalent to about 0·006 per cent. of the weight of the root.

*Non-volatile Constituents of the Extract.*

After the above-described operation, there remained in the distillation flask a dark-coloured, aqueous liquid (A), and a considerable quantity of a black resin (B). These products were separated by filtration, and the resin thoroughly washed with water, the washings being added to the main portion of the aqueous liquid.

*Examination of the Aqueous Liquid (A).*

The aqueous liquid was concentrated under diminished pressure to a convenient volume, and then repeatedly extracted with ether. A small amount (4·5 grams) of a viscid, brown oil was thus removed, which, however, with the exception of traces of a weak base, yielded nothing of interest.

The aqueous liquid was next shaken repeatedly with amyl alcohol. This solvent extracted a considerable quantity of a yellow, amorphous product, which, on exposure to the atmosphere, rapidly absorbed moisture, and became glutinous. This yellow solid could not be obtained crystalline, nor could any crystalline derivative be prepared from it. It was not glucosidic.

The aqueous liquid was subsequently treated with a slight excess of basic lead acetate, when a voluminous, light brown precipitate was obtained. The lead precipitate, which contained nothing of an alkaloidal nature, was examined in the usual way, but yielded only indefinite substances, giving the reactions for tannin. The filtrate from the basic lead acetate precipitate was treated with hydrogen sulphide for the removal of the lead, and the mixture filtered. The concentrated filtrate was yellow in colour, and contained a considerable quantity of sugar, since it readily yielded *d*-phenylglucosazone, melting and decomposing at 210°. On heating the liquid with alkali hydroxide, it developed ammonia, and it also yielded precipitates with the usual alkaloid reagents, but these reactions were evidently due to soluble protein products, since the alkaline liquid, when extracted with either chloroform or amyl alcohol, yielded nothing of a definitely alkaloidal nature.

*Examination of the Resin (B).*

The resin amounted to 502 grams, being thus equivalent to about 2·7 per cent. of the weight of the root. It was digested with hot

alcohol, the solution poured upon purified sawdust, and the dried mixture extracted successively in a Soxhlet apparatus with light petroleum, ether, chloroform, ethyl acetate, and alcohol.

*Petroleum Extract of the Resin.*

This was a dark-coloured, soft solid, which amounted to 138 grams. It was heated in a reflux apparatus with an excess of an alcoholic solution of potassium hydroxide, the greater portion of the alcohol then removed, water added, and the alkaline mixture extracted with ether. On evaporating the solvent, a quantity (37 grams) of a brown, viscid product was obtained, which was found to contain some basic substance. It was therefore re-dissolved in ether, and the ethereal solution shaken with dilute hydrochloric acid. The acid liquid was then carefully neutralised with sodium carbonate, when a colourless precipitate, amounting to about 0·1 gram, was deposited. This substance, when recrystallised from dilute alcohol, separated in colourless, glistening leaflets, melting at 116°, and was found to be identical with the base,  $C_{12}H_{16}N_2$ , subsequently to be described in connexion with the examination of the ether extract of the resin. As will be shown later, it is probable that the above compound is not originally present in the resin, but was formed from an alkaloidal constituent by the treatment with alcoholic potassium hydroxide.

*Isolation of Hentriacontane,  $C_{21}H_{44}$ , and a Phytosterol,  $C_{27}H_{46}O$ .*

The ethereal solution, which had been shaken with hydrochloric acid for the removal of the base, as described above, was washed, dried, and the solvent evaporated. The residue was then fractionally crystallised from a mixture of ethyl acetate and alcohol. The more sparingly soluble deposits, when crystallised from ethyl acetate, were obtained in glistening leaflets, melting at 67–68°, and proved to be hentriacontane. (Found, C=85·2; H=14·5. Calc., C=85·3; H=14·7 per cent.)

After the removal of the greater part of the hentriacontane in the above fractionation, the mother liquors gradually deposited a small quantity of a substance in flat plates. This was purified by recrystallisation from ethyl acetate, and it then melted at 135–136°:

0·1113 \* gave 0·3420  $CO_2$  and 0·1202  $H_2O$ . C=83·8; H=12·0.  
 $C_{27}H_{46}O$  requires C=83·9; H=11·9 per cent.

This substance was evidently a phytosterol, and it gave the colour reaction of that class of compounds.

\* Anhydrous substance.

*The Fatty Acids.**Isolation of Cerotic Acid, C<sub>26</sub>H<sub>52</sub>O<sub>2</sub>.*

The alkaline, aqueous solution of potassium salts, which had been extracted with ether for the removal of the unsaponifiable material, as above described, was acidified with sulphuric acid, and extracted with ether. On evaporating the ethereal solution, it yielded 15 grams of a dark green, soft solid, which evidently contained a considerable amount of resinous matter. The latter was separated by washing with petroleum, in which the resin was insoluble. The mixed fatty acids obtained from the petroleum washings were converted into their methyl esters, and the latter distilled under diminished pressure. Two fractions were collected, the one distilling at 205—230°/28 mm., and the other above 230°/28 mm. The latter fraction, consisting of a wax-like solid, yielded, on hydrolysis, an acid which, on recrystallisation from alcohol, separated in clusters of colourless leaflets, melting at 71—72°, and was identified as cerotic acid (Found, C=78·7; H=13·2. Calc., C=78·8; H=13·1 per cent.), the somewhat low melting point being probably due to a slight impurity.

The above-mentioned fraction, which distilled at 205—230°/28 mm., contained a considerable proportion of unsaturated esters. The entire fraction was therefore hydrolysed, and the resulting fatty acids separated by means of their lead salts into saturated and unsaturated portions. The saturated acids, amounting to 5·5 grams, were crystallised from alcohol, and thus separated into two fractions of different solubilities. Each of these fractions melted at 52—54°, but they possessed neutralisation values of 210 and 201 respectively, and it was thus evident that the saturated acids consisted of a mixture of palmitic and stearic acids.

The unsaturated acids, which amounted to 4·8 grams, were distilled under diminished pressure, when they passed over at 220—240°/20 mm. An analysis and a determination of the iodine value gave the following results:

0·1391 gave 0·3916 CO<sub>2</sub> and 0·1462 H<sub>2</sub>O. C=76·8; H=11·7.

0·1711 absorbed 0·2260 iodine. Iodine value=132·1.

C<sub>18</sub>H<sub>34</sub>O<sub>2</sub> requires C=76·6; H=12·1 per cent. Iodine value=90·1.  
C<sub>18</sub>H<sub>32</sub>O<sub>2</sub> " C=77·1; H=11·4 " Iodine value=181·4.

These results indicate that the unsaturated acids consisted of a mixture of oleic and linolic acids in approximately equal proportions.

*Ethereal Extract of the Resin.**Isolation of Ipuranol, C<sub>23</sub>H<sub>38</sub>O<sub>2</sub>(OH)<sub>2</sub>.*

The ether extract of the resin was a black, brittle solid, amounting to 42·7 grams. It was digested with a large volume of ether, when about 4 grams of a light green, solid substance remained undissolved. The latter was collected, and purified by several crystallisations from pyridine containing a little water, when it was obtained in colourless, microscopic needles, melting and decomposing at 290—300°:

0·1103 gave 0·2929 CO<sub>2</sub> and 0·1021 H<sub>2</sub>O. C = 72·4; H = 10·3.  
C<sub>23</sub>H<sub>38</sub>O<sub>4</sub> requires C = 72·6; H = 10·5 per cent.

When the substance was dissolved in chloroform with a little acetic anhydride, and a drop of concentrated sulphuric acid subsequently added, a transient pink colour, changing to blue and then to green, was produced. The compound also yielded an acetyl derivative, melting at 164—165°, and it was thus definitely identified as ipuranol.

The ethereal solution from which the sparingly soluble ipuranol had been removed, as above described, was extracted successively with aqueous ammonium carbonate, sodium carbonate, and sodium hydroxide. These extracts, however, on acidification, yielded only resinous material. On evaporating the greater portion of the ether, a small quantity of a crystalline compound separated, which, when purified by crystallisation from a mixture of alcohol and chloroform, separated in thin, colourless needles, melting and decomposing at 300°. It was found to be identical with the new compound, withaniol, C<sub>25</sub>H<sub>34</sub>O<sub>5</sub>, which was obtained in larger amount from the chloroform extract of the resin.

*Isolation of an Alkaloidal Principle.*

The ethereal filtrate from the above-described crystalline substance contained a compound which gave precipitates with the usual alkaloid reagents. The alkaloidal principle was not soluble in dilute acids, but was extracted from the ethereal liquid by repeatedly shaking with concentrated hydrochloric acid. The acid liquids were then carefully neutralised with sodium carbonate, when an amorphous solid was precipitated, which was taken up with chloroform. The chloroform extract, after washing and drying, yielded 1·5 grams of a weak, gum-like base, which could not be obtained in a crystalline state. It gave a yellow, amorphous gold salt, melting and decomposing at 185°.

*Action of Potassium Hydroxide on the Alkaloid. Isolation of a Crystalline Base, C<sub>12</sub>H<sub>16</sub>N<sub>2</sub>.*

A portion of the above-described alkaloid was heated for an hour with an alcoholic solution of potassium hydroxide. The alcohol was then removed, water added, and the alkaline liquid extracted with ether. The ethereal solution was then shaken with dilute hydrochloric acid, and the acid liquid neutralised with aqueous sodium carbonate, when a small amount (0·2 gram) of a colourless solid was precipitated. This substance was crystallised from dilute alcohol, and was thus obtained in colourless, glistening leaflets, melting at 116°:

0·0792 gave 0·2230 CO<sub>2</sub> and 0·0597 H<sub>2</sub>O. C = 76·8; H = 8·4.  
0·0655 „ 8·5 c.c. moist N<sub>2</sub> (over KOH) at 14° and 760 mm.  
N = 15·3.

C<sub>12</sub>H<sub>16</sub>N<sub>2</sub> requires C = 76·6; H = 8·5; N = 14·9 per cent.

The above-described substance would thus appear to possess the empirical formula C<sub>12</sub>H<sub>16</sub>N<sub>2</sub>, and, as it differs in its properties from any substance of this formula which has hitherto been recorded, it is evidently a new compound.

The base, C<sub>12</sub>H<sub>16</sub>N<sub>2</sub>, is readily soluble in alcohol, ethyl acetate, ether, chloroform, or benzene, but only sparingly soluble in light petroleum or hot water. It is neutral towards litmus, but is easily dissolved by an excess of dilute mineral acids. When heated in an ignition tube, it first melts, and then sublimes unchanged.

The *hydrochloride* was prepared by adding to an ethereal solution of the base a drop of concentrated hydrochloric acid. A crystalline solid was thus deposited, which, when recrystallised from a mixture of ether and alcohol, separated in thin, colourless needles, sintering at 190°, and melting at 201°. The *pierate* crystallised from hot water, in which it is only moderately soluble, in silky, yellow needles, melting at 171°.

After the removal of the crystalline base from the product of the above reaction, the alkaline liquid yielded, on acidification, a small quantity of a solid substance, which, however, could not be obtained crystalline.

*Chloroform Extract of the Resin.*

*Isolation of a New Monohydric Alcohol, Withanol, C<sub>23</sub>H<sub>32</sub>O<sub>4</sub>·OH.*

The portion of the resin extracted by chloroform was relatively large, amounting to 123 grams. It was redissolved in chloroform, and the solution extracted with aqueous ammonium carbonate, sodium carbonate, and sodium hydroxide, each of which removed

some amorphous, resinous material. The chloroform solution was then washed, dried, and the solvent removed, when a viscid, brown residue was obtained, which, on agitation with alcohol, deposited a colourless, crystalline compound. This compound, amounting to 5 grams, was collected, and recrystallised from a mixture of chloroform and alcohol, when it separated in colourless needles, which sintered at 285° and completely decomposed at 305°:

0·1081 gave 0·2866 CO<sub>2</sub> and 0·0816 H<sub>2</sub>O. C=72·2; H=8·4.

0·1022, " 0·2703 CO<sub>2</sub>, " 0·0750 H<sub>2</sub>O. C=72·1; H=8·2.

The molecular weight of the substance was determined by the cryoscopic method:

0·3170, in 28·16 nitrobenzene, gave Δt = -0·191°. M.W. = 412.

C<sub>25</sub>H<sub>34</sub>O<sub>5</sub> requires C=72·5; H=8·2 per cent. M.W. = 414.

No compound of the empirical formula C<sub>25</sub>H<sub>34</sub>O<sub>5</sub>, possessing properties identical with those of the above substance, has hitherto been described. It is therefore proposed to designate the new compound *withaniol*, with reference to the generic name of the plant from which it has been obtained.

*Withaniol*, C<sub>25</sub>H<sub>34</sub>O<sub>5</sub>, is readily soluble in chloroform, only moderately so in alcohol, and practically insoluble in ether or light petroleum. It dissolves in cold concentrated hydrochloric acid, and is precipitated unchanged on the addition of water. It undergoes some change when heated with alkalis in the presence of alcohol, since the solution becomes deep red, and deposits, on acidification, a red, amorphous precipitate. When dissolved in a mixture of acetic anhydride and chloroform, and a drop of concentrated sulphuric acid subsequently added, a pink coloration appears, which gradually changes to a straw-yellow colour.

Withaniol is optically active, a determination of its rotatory power giving the following result:

0·3745, made up to 20 c.c. with chloroform, gave  $\alpha_D + 3^{\circ}15'$  in a 2-dcm. tube, whence  $[\alpha]_D + 91\cdot2^\circ$ .

Withaniol contains no methoxy-group, but the presence of one hydroxyl group was proved by the formation of a monoacetyl derivative.

*Acetylwithaniol*, C<sub>25</sub>H<sub>33</sub>O<sub>5</sub>CO·CH<sub>3</sub>.—This derivative was prepared by heating withaniol for some time with an excess of acetic anhydride. On cooling the solution, the *acetyl* compound was deposited in the form of colourless, prismatic needles. After recrystallisation from acetic anhydride, it began to melt at 280°, and at 300° became completely decomposed:

0·1032 gave 0·2675 CO<sub>2</sub> and 0·0750 H<sub>2</sub>O. C=70·7; H=8·1.

0·1122, " 0·2920 CO<sub>2</sub>, " 0·0832 H<sub>2</sub>O. C=71·0; H=8·2.

C<sub>25</sub>H<sub>33</sub>O<sub>5</sub>CO·CH<sub>3</sub> requires C=71·1; H=7·9 per cent.

*Ethyl Acetate Extract of the Resin.*

This was a black, brittle solid, amounting to 26·8 grams. It was heated for several hours with dilute sulphuric acid in aqueous alcohol, when, after removing the alcohol, an amorphous resin separated, and a yellow, aqueous liquid was obtained which readily reduced Fehling's solution. The presence of sugar in the aqueous liquid was confirmed by the formation of *d*-phenylglucosazone, melting and decomposing at 210°. It is thus evident that the ethyl acetate extract of the resin was glucosidic in character.

*Alcohol Extract of the Resin.*

This resin amounted to 105 grams, and consisted of a hard, black solid. A preliminary examination having indicated the presence of a glucosidic substance, the whole of the resin was heated for several hours with dilute sulphuric acid in aqueous alcohol. After the removal of the alcohol, the mixture was distilled in a current of steam, but no volatile product of hydrolysis was obtained. There then remained in the distillation flask a quantity of resin and a reddish-brown, aqueous liquid, which was separated by filtration. The resin yielded nothing crystalline, but the aqueous liquid, when rendered alkaline by means of sodium hydroxide, deposited about 1 grain of a dark brown, gelatinous product. This was collected, found to contain nitrogen, and to possess weakly basic properties. It was, however, of a very indefinite character, and could not be obtained crystalline, nor could any crystalline salt be prepared from it. When heated with aqueous potassium hydroxide, a strong ammoniacal odour was developed.

The aqueous liquid, from which the above-described basic substance had been removed, readily reduced Fehling's solution, and yielded *d*-phenylglucosazone, melting and decomposing at 205°. It is thus apparent that at least a portion of the alcohol extract of the resin was of a glucosidic nature.

## II. Examination of the Leaves and Stems.

As a preliminary experiment, a small portion of the ground material was tested for the presence of an alkaloid, and with a positive result.

For the purpose of a complete examination, 6·97 kilograms of the dried leaves and stems were ground, and extracted by continuous percolation with hot alcohol. The greater part of the alcohol was then removed, the residual extract (2·24 kilograms) mixed with water, and the mixture distilled in a current of steam. The

distillate contained a very small quantity (0.2 gram) of an essential oil, possessing a strong, pungent odour.

After the above-described operation, there remained in the distillation flask a brown, aqueous liquid, containing a quantity of resin. These products were separated by decantation, and the resin well washed with boiling water, the washings being added to the main volume of aqueous liquid.

#### *Examination of the Aqueous Liquid.*

The aqueous liquid was concentrated under diminished pressure to a convenient bulk, then repeatedly extracted with ether, and finally with amyl alcohol. These solvents, however, removed only small quantities of gummy material, which, in each case, was found to contain a trace of a weak amorphous base. The latter, although responding to the usual tests for an alkaloid, was very indefinite in character, and yielded no crystalline salt. No glucosidic substance was present.

The aqueous liquid which had been extracted with the above-mentioned solvents was subsequently treated with an excess of basic lead acetate, which removed tannin and colouring matter. The filtrate from the basic lead acetate precipitate was deprived of lead and concentrated under diminished pressure to a small volume, when, on cooling, a considerable quantity of potassium nitrate was deposited. The filtrate from the latter still gave a precipitate with alkaloid reagents, and also contained some sugar, since it readily yielded *d*-phenylglucosazone, decomposing at 205°. The aqueous liquid was finally rendered alkaline and extracted successively with ether and chloroform, but these solvents removed only very small quantities of a gummy, basic substance, which yielded no crystalline derivative.

#### *Examination of the Resin.*

The resin was a dark green powder, and amounted to 624 grams. It was dissolved in hot alcohol, mixed with purified sawdust, and the thoroughly dried mixture extracted successively in a Soxhlet apparatus with light petroleum, ether, chloroform, ethyl acetate, and alcohol.

#### *Petroleum Extract of the Resin.*

This extract was a dark green, soft solid, amounting to 67 grams. It was dissolved in ether, and the solution shaken with both dilute and strong hydrochloric acid, but no basic substance was thus removed.

*Isolation of Hentriaccontane, C<sub>31</sub>H<sub>64</sub>, and a Phytosterol, C<sub>27</sub>H<sub>46</sub>O.*

The above-mentioned ethereal liquid was next distilled for the removal of the solvent, and the residue heated with an alcoholic solution of potassium hydroxide. After the removal of the alcohol, water was added, and the alkaline liquid completely extracted with ether. The ethereal extract yielded 26 grams of a semi-solid product, which was fractionally crystallised from ethyl acetate, when a colourless compound, separating in glistening leaflets and melting at 68°, was obtained. This substance, amounting to 5 grams, was identified as hentriaccontane (Found, C=85·1; H=14·7. Calc., C=85·3; H=14·7 per cent.).

The mother-liquors from the above crystallisations were united, the solvent removed, and the residue fractionally distilled under diminished pressure. The lower-boiling fractions contained a considerable quantity of hentriaccontane, but the final fraction, after several crystallisations from hot alcohol, yielded a compound crystallising in flat plates, which melted at 133°, and gave the colour reaction of the phytosterols:

0·0883 gave 0·2720 CO<sub>2</sub> and 0·0940 H<sub>2</sub>O. C=84·0; H=11·8.  
C<sub>27</sub>H<sub>46</sub>O requires C=83·9; H=11·9 per cent.

This substance was thus proved to be a phytosterol, and it was apparently identical with that obtained from the root.

*The Fatty Acids.**Isolation of Cerotic Acid, C<sub>26</sub>H<sub>52</sub>O<sub>2</sub>.*

The alkaline liquid from which the above-mentioned hentriaccontane and phytosterol had been removed was acidified with sulphuric acid, and the precipitated fatty acids taken up with ether. The ethereal solution, on the evaporation of the solvent, yielded a semi-solid residue of fatty acids, which were converted into their methyl esters, and the latter then fractionally distilled under diminished pressure. The greater portion passed over at 205–215°/12 mm., but a small fraction was collected above 215°/12 mm., and a considerable quantity of non-volatile resinous material remained in the distillation flask. The fraction distilling above 215°/12 mm. solidified in the receiver, and, when recrystallised from alcohol, was obtained in glistening leaflets, melting at 56–57°. This product consisted of methyl cerotate (m. p. 80°), since on hydrolysis it yielded an acid which separated from ethyl acetate in stellar aggregates of fine needles, melting at 76–77° (Found, C=78·6; H=13·3. Calc., C=78·8; H=13·1 per cent.).

The fraction of methyl esters distilling at 205—215°/12 mm. was hydrolysed, and the regenerated acids separated by means of their lead salts into saturated and unsaturated portions. The saturated acids were found to melt at 49—51°, and to possess a neutralisation value of 205°. After one crystallisation from alcohol, the melting point was 51—53° and the neutralisation value 207°. It was thus evident that the saturated acids consisted of a mixture of palmitic and stearic acids, which possess neutralisation values of 219 and 198 respectively.

The unsaturated acids were distilled under diminished pressure, when they passed over at 220—235°/15 mm. An analysis and a determination of the iodine value gave the following results:

0·1033 gave 0·2912 CO<sub>2</sub> and 0·1075 H<sub>2</sub>O. C=76·9; H=11·6.

0·1306 absorbed 0·2086 iodine. Iodine value=159·7.

C<sub>18</sub>H<sub>34</sub>O<sub>2</sub> requires C=76·6; H=12·1 per cent. Iodine value=90·1.

C<sub>18</sub>H<sub>32</sub>O<sub>2</sub>    "    C=77·1; H=11·4    "    Iodine value=181·4.

The unsaturated acids would thus appear to have consisted of a mixture of oleic and linolic acids, the latter preponderating.

#### *Ethereal Extract of the Resin.*

##### *Isolation of Ipuranol, C<sub>25</sub>H<sub>38</sub>O<sub>2</sub>(OH)<sub>2</sub>.*

This extract was obtained in the form of a light green powder, amounting to 156 grams. On digesting the extract with ether, it was observed that a portion of it was very sparingly soluble. This was therefore separated by filtration from the more readily soluble portion, which amounted to 60 grams, and consisted of chlorophyll and indefinite amorphous substances. The portion sparingly soluble in ether was subsequently digested with hot alcohol, when a small quantity of a light green solid remained undissolved. The latter was collected, and, after crystallisation from dilute pyridine, was found to decompose at 285—290°, and to give the colour reaction of ipuranol. Its complete identification was effected by means of the acetyl derivative, which melted at 164—165°, and when mixed with a known specimen of acetylipuranol the melting point remained unchanged.

##### *Isolation of a New Monoxydric Alcohol, Somnirol, C<sub>32</sub>H<sub>48</sub>O<sub>6</sub>·OH.*

The above-mentioned alcoholic solution of the sparingly soluble portion of the ether extract of the resin was heated to boiling, and sufficient water added to produce a faint cloudiness. On cooling, a quantity of an oily resin separated, which gradually became semi-solid. This was collected and put aside for subsequent examination. By the further cautious addition of water

to the hot mother-liquors, the greater portion of the oleo-resinous material was removed, after which a crystalline substance began to be deposited. The latter was then purified by several recrystallisations from dilute alcohol, when it was obtained in colourless, prismatic needles in an amount of 3 grams:

0·5981, dried at 110°, lost 0·0364 H<sub>2</sub>O. H<sub>2</sub>O = 6·1.  
 0·0975\* gave 0·2542 CO<sub>2</sub> and 0·0748 H<sub>2</sub>O. C = 71·1; H = 8·5.  
 0·1126\* „ 0·2882 CO<sub>2</sub> „ 0·0834 H<sub>2</sub>O. C = 71·0; H = 8·4.  
 0·1136\* „ 0·2968 CO<sub>2</sub> „ 0·0844 H<sub>2</sub>O. C = 71·3; H = 8·2.  
 $C_{32}H_{44}O_7 \cdot 2H_2O$  requires H<sub>2</sub>O = 6·2 per cent.  
 $C_{32}H_{44}O_7$  requires C = 71·1; H = 8·1 per cent.

The molecular weight of the substance was determined by the cryoscopic method with the following result:

0·5496\*, in 31·52 nitrobenzene, gave  $\Delta t = -0·225^\circ$ . M.W. = 542.  
 $C_{32}H_{44}O_7$  requires M.W. = 540.

No substance identical with the above compound appears to have hitherto been described. It is therefore proposed to designate the new compound *somnirol*, with reference to its alcoholic properties and the specific name of the plant from which it has been isolated.

*Somnirol*,  $C_{32}H_{43}O_6 \cdot OH$ , is very soluble in alcohol, ethyl acetate, or chloroform, only moderately soluble in benzene, and very sparingly so in ether. It crystallises from dilute alcohol with two molecules of water of crystallisation, which are expelled at 110°, but are again rapidly absorbed when the anhydrous substance is exposed to the atmosphere. The behaviour of the substance on heating is characteristic, inasmuch as it partly melts at about 155° with effervescence and immediate resolidification, and then finally fuses with evolution of gas at 205°.

A determination of the optical rotatory power of somnirol gave the following result:

0·1796\*, made up to 25 c.c. with chloroform, gave  $\alpha_D + 0^\circ 30'$  in a 2-dm. tube, whence  $[\alpha]_D + 34^\circ 8'$ .

Somnirol contains no methoxyl, and, as shown below, only one hydroxyl group. In order to obtain some further information respecting the character of the substance, a portion of it was heated with decinormal alcoholic potassium hydroxide:

0·2002, heated for 20 minutes, neutralised 0·0222 KOH.  
 KOH = 11·1 per cent.

0·2271, heated for one hour, neutralised 0·0275 KOH.  
 KOH = 12·1 per cent.

$C_{32}H_{44}O_7$ , to neutralise 1 mol. KOH, requires KOH = 10·4 per cent.

With the object of isolating, if possible, the products of the

\* Anhydrous substance.

above reaction, a quantity (0·5 gram) of somnirol was heated for a short time with alcoholic potassium hydroxide. The alcohol was then removed and water added, but no precipitation ensued, nor could any product be isolated from the alkaline solution by extraction with ether or chloroform. The alkaline liquid, on acidification, deposited a gelatinous precipitate, which, after collecting and drying, was found to be only imperfectly soluble in alkalis, and almost insoluble in the ordinary organic solvents. From these results it may be concluded that somnirol contains at least one lactonic grouping.

*Acetyl somnirol*,  $C_{22}H_{33}O_7 \cdot CO \cdot CH_3$ .—This compound was prepared by heating somnirol for an hour with acetic anhydride, the greater portion of the latter being then removed by distillation, and water added, when the *acetyl* derivative was precipitated as an oil, which gradually became solid. The product was collected, dried in a vacuum over sulphuric acid, and dissolved in hot benzene, from which it was deposited in colourless, torpedo-shaped crystals. The latter contained benzene of crystallisation, which was not lost on keeping the compound for some time in a vacuum over sulphuric acid, and was only very slowly expelled on heating at 100°. When heated in a capillary tube, the air-dried substance begins to change at about 115°, and apparently melts at 125° with evolution of gas. Heated to 110° on a watch-glass, the substance gradually melts, bubbles of gaseous benzene are evolved, and it then resolidifies to a hard, brittle, transparent mass. On recrystallising the latter from benzene, the original compound, containing that solvent, was obtained:

0·1178 gave 0·3157  $CO_2$  and 0·0859  $H_2O$ . C=73·1; H=8·1.

$C_{22}H_{33}O_7 \cdot CO \cdot CH_3 \cdot C_6H_6$  requires C=72·7; H=7·9 per cent.

The benzene-free acetyl derivative was next analysed:

0·1369 gave 0·3510  $CO_2$  and 0·0994  $H_2O$ . C=69·8; H=8·1.

0·0801 „ 0·2050  $CO_2$  „ 0·0586  $H_2O$ . C=69·8; H=8·1.

$C_{22}H_{33}O_7 \cdot CO \cdot CH_3$  requires C=70·1; H=7·9 per cent.

#### *Isolation of a New Dihydric Alcohol, Samnitol, $C_{33}H_{44}O_5(OH)_2$ .*

The dilute alcoholic mother-liquors remaining after the separation of the somnirol, as above described, still contained a considerable amount of substance in solution. On removing the alcohol in a current of steam, an oily substance was deposited, which gradually solidified. The solid was collected, dried in a vacuum over sulphuric acid, and then digested with ethyl acetate. This treatment removed the remaining somnirol, and left a sparingly soluble compound, which was recrystallised from alcohol. It separated from

this solvent in thin, hair-like needles, which sintered at 240°, and melted and decomposed at about 250°. The yield of this substance was 4 grams:

0·4704, dried at 110°, lost 0·0310 H<sub>2</sub>O. H<sub>2</sub>O = 6·6.  
 0·1160\* gave 0·3037 CO<sub>2</sub> and 0·0898 H<sub>2</sub>O. C = 71·4; H = 8·6.  
 0·1071\*, 0·2805 CO<sub>2</sub>, 0·0830 H<sub>2</sub>O. C = 71·4; H = 8·6.  
 C<sub>33</sub>H<sub>46</sub>O<sub>7</sub>.2H<sub>2</sub>O requires H<sub>2</sub>O = 6·1 per cent.  
 C<sub>33</sub>H<sub>46</sub>O<sub>7</sub> requires C = 71·5; H = 8·3 per cent.

A molecular-weight determination by the cryoscopic method gave the following result:

0·2454,\* in 33·80 nitrobenzene, gave Δt = -0·092°. M.W. = 553.  
 C<sub>33</sub>H<sub>46</sub>O<sub>7</sub> requires M.W. = 554.

No compound of the above formula appears to have previously been described. It is therefore proposed to designate the substance *somnitol*, with reference to its alcoholic character and the specific name of the plant from which it has been obtained.

*Somnitol* is practically insoluble in water, and only moderately soluble in hot absolute alcohol. It dissolves readily in chloroform and in dilute alcohol, separating from the latter solvent with 2 molecules of water. The compound is optically active, a determination of its rotatory power giving the following result:

0·3940,\* made up to 25 c.c. with chloroform, gave α<sub>D</sub> + 0°31' in a 2-dm. tube, whence [α]<sub>D</sub> + 21·9°.

When somnitol is heated with alkali hydroxides in alcoholic solution it slowly undergoes change, and the liquid acquires a deep red colour, but even after prolonged heating with concentrated alkali a part of the compound was recovered unaltered. The reaction is therefore not comparable with that which takes place when somnirol is similarly treated, since in the latter case no trace of unchanged substance can be detected, even after a few minutes heating with the alkali.

Somnitol contains no methoxyl, but was found to possess two hydroxyl groups, since it readily yields a diacetyl derivative.

*Diacetyl somnitol*, C<sub>33</sub>H<sub>44</sub>O<sub>7</sub>(CO·CH<sub>3</sub>)<sub>2</sub>.—This compound was prepared by heating somnitol with acetic anhydride for an hour. On concentrating the solution, an *acetyl* derivative separated in colourless prisms, which, after recrystallisation from acetic anhydride, melted and decomposed at 270–275°. It was practically insoluble in cold acetic anhydride or alcohol, but readily soluble in chloroform:

0·1127 gave 0·2866 CO<sub>2</sub> and 0·0841 H<sub>2</sub>O. C = 69·4; H = 8·3.  
 0·1056, 0·2693 CO<sub>2</sub>, 0·0782 H<sub>2</sub>O. C = 69·6; H = 8·2.

C<sub>33</sub>H<sub>44</sub>O<sub>7</sub>(CO·CH<sub>3</sub>)<sub>2</sub> requires C = 69·6; H = 7·8 per cent.

\* Anhydrous substance.

*Isolation of an Acidic, Hydrolytic Product: Withanic Acid,  
 $C_{29}H_{45}O_6 \cdot CO_2H$ .*

The oily resin which had separated from the alcoholic solution of the ether extract of the resin by the first addition of water, as above described, was next examined, but no crystalline compound could be directly isolated from it. It was therefore heated for a short time with an alcoholic solution of potassium hydroxide, the alcohol then removed, and the product of hydrolysis extracted successively with ether and chloroform, which, however, removed nothing. On acidifying the alkaline liquid, a gelatinous precipitate was formed, the greater part of which was insoluble in organic solvents, but a small portion was soluble in hot alcohol, from which it crystallised in colourless, tetrahedral prisms, melting and decomposing at  $226^\circ$ :

0·1124, dried at  $110^\circ$ , lost 0·0038 H<sub>2</sub>O. H<sub>2</sub>O = 3·1.

0·1136\* gave 0·2796 CO<sub>2</sub> and 0·0904 H<sub>2</sub>O. C = 67·1; H = 8·8.

$C_{30}H_{46}O_8 \cdot H_2O$  requires H<sub>2</sub>O = 3·3 per cent.

$C_{29}H_{45}O_8$  requires C = 67·4; H = 8·6 per cent.

This substance was readily soluble in alkalis, including ammonium carbonate, and when titrated with a decinormal alcoholic solution of sodium hydroxide gave the following result:

0·2060 neutralised 3·8 c.c. N/10-NaOH. M.W. (monobasic acid) = 542.

$C_{29}H_{45}O_6 \cdot CO_2H$  requires M.W. = 534.

As the above-described acid is evidently a new compound, it is proposed to designate it *withanic acid*.

*Withanic acid*,  $C_{30}H_{46}O_8$ , is very sparingly soluble in ether, chloroform, or benzene, and only moderately soluble in boiling alcohol. Its *methyl ester*, prepared by heating the substance with methyl alcohol in presence of concentrated sulphuric acid, was very soluble in alcohol or acetone, but could be crystallised from a mixture of acetone and benzene, when it separated in hard, crystalline nodules, sintering at  $240^\circ$ , and decomposing with effervescence at  $255^\circ$ .

*Chloroform Extract of the Resin.*

This consisted of a light green powder, which amounted to 212 grams. As nothing could be directly isolated from this material, it was heated with dilute sulphuric acid in aqueous alcohol. On subsequently rendering the liquid alkaline, about 1 gram of an almost colourless, glutinous solid separated, which

\* Anhydrous substance.

was found to contain nitrogen, but which could not be obtained crystalline nor did it yield any crystalline salt.

The chloroform extract of the resin was also tested for the presence of a glucoside, but with a negative result.

*Ethyl Acetate and Alcohol Extracts of the Resin.*

The ethyl acetate extract of the resin amounted to only 10 grams. It was found to contain some glucosidic material, since on heating with dilute sulphuric acid in aqueous alcohol it yielded a sugar from which *d*-phenylglucosazone (m. p. 205°) was prepared.

The alcohol extract of the resin, consisting of a hard, brittle solid, amounted to 94 grams. It was glucosidic in character, and on heating for several hours with dilute sulphuric acid in aqueous alcohol it also yielded a small amount of an indefinite basic substance, the properties of which were very similar to those of the substance obtained from the chloroform extract of the resin.

*Summary.*

The material employed for this investigation represented the entire plant of *Withania somnifera*, Dunal (Nat. ord. *Solanaceae*), and was obtained directly from South Africa. The root and the overground portion of the plant, consisting of the leaves and stems, were separately examined.

Preliminary tests, conducted with both portions of the plant, indicated the presence of an alkaloid.

I. *Constituents of the Root.*—An alcoholic extract of the root, when distilled with steam, yielded a very small amount of an essential oil. The portion of the extract which was soluble in water contained, besides indefinite, amorphous substances, a quantity of sugar, which yielded *d*-phenylglucosazone (m. p. 210°).

The portion of the extract which was insoluble in water consisted chiefly of a black resin, and amounted to about 2·7 per cent. of the weight of the root. From this resin the following definite substances were isolated: hentriacontane,  $C_{31}H_{64}$ ; a phytosterol,  $C_{27}H_{46}O$  (m. p. 135—136°); a mixture of fatty acids, consisting of palmitic, stearic, cerotic, oleic, and linolic acids; ipuranol,  $C_{25}H_{50}O_2(OH)_2$ ; a new monohydric alcohol, *withanol*,  $C_{23}H_{38}O_1OH$ , decomposing at 305°, and having  $[\alpha]_D + 91\cdot2^\circ$ ; and an amorphous, alkaloidal principle, which, on treatment with alkalis, yielded a crystalline base,  $C_{12}H_{16}N_2$  (m. p. 116°).

II. *Constituents of the Leaves and Stems.*—An alcoholic extract of this material, when submitted to distillation with steam, yielded a very small amount of an essential oil. The portion of the extract which was soluble in water contained, besides tannin and colouring

matter, a sugar yielding *d*-phenylglucosazone (*m. p.* 205°), and a considerable quantity of potassium nitrate.

The portion of the extract which was insoluble in water consisted chiefly of resinous material, and was obtained in the form of a dark green powder. This resin was found to contain a number of substances which had also been isolated from the root of the plant, such as hentriacontane, a phytosterol,  $C_{27}H_{46}O$  (*m. p.* 133°), a mixture of fatty acids, and ipuranol. In addition to these, however, it yielded the following compounds: a new monohydric alcohol, *somnitol*,  $C_{32}H_{48}O_6 \cdot OH$ , decomposing at 205° and having  $[\alpha]_D + 34.8^\circ$ ; a new dihydric alcohol, *somnitol*,  $C_{33}H_{44}O_5(OH)_2$ , decomposing at about 250°, and having  $[\alpha]_D + 21.2^\circ$ ; and an acidic, hydrolytic product, *withanic acid*,  $C_{29}H_{42}O_6 \cdot CO_2H$  (*m. p.* 226°), the methyl ester of which decomposed at 255°.

Inasmuch as the *Withania somnifera*, unlike some other solanaceous plants, had been found to contain no mydriatic alkaloid, it was deemed of interest to ascertain whether the sedative or hypnotic properties attributed to it could be confirmed. For this purpose, some tests were kindly conducted for us at the Wellcome Physiological Research Laboratories by Drs. H. H. Dale and P. P. Laird, to whom our thanks are due. It was thus ascertained that alcoholic extracts, representing about 7 grams of the root and 3 grams of the leaves and stems respectively, when administered to a dog had no perceptible effect. The hypodermic injection of the alkaloidal principle obtained from the root likewise produced in a dog no symptom of narcosis or other definite result.

THE WELLCOME CHEMICAL RESEARCH LABORATORIES,  
LONDON, E.C.

## LX.—*The Constancy of Water of Crystallisation in Hydrated Salts. Part I.*

By HERBERT BRERETON BAKER and GEORGE HENRY JOSEPH ADLAM.

THE use of salts containing water of crystallisation for accurate work, such as the determination of atomic weights, has been a subject of discussion for many years. According to Richards (*Zeitsch. physikal. Chem.*, 1904, **46**, 216), such salts always contain an excess of water, supposed to be occluded in some way in the mass of the crystal. Marckwald (*Ber.*, 1907, **40**, 4730) published a paper in 1907 on the atomic weight of tellurium, in which he

concluded that the true atomic weight was below that of iodine, solely on the evidence obtained from the decomposition of telluric acid ( $H_2TeO_4 \cdot 2H_2O$ ). This work was criticised by one of us ( Baker, *Chem. News*, 1908, **97**, 209), both on general grounds, and also because a long series of experiments with the same substance had pointed to the impossibility of obtaining the crystals of constant composition. Marchwald \* has recently withdrawn his assertion of the low atomic weight, since by using a more trustworthy method for the determination he has obtained results which confirm the number found by other investigators. It was in reference to telluric acid that this work was begun, but other cases have been studied.

In the cases which we have investigated, it has been found that there is, as Richards proved for barium chloride, an excess of water over the calculated amount. Richards (*loc. cit.*) considers that this water is occluded in cavities in the crystal, since by reducing the substance to varying degrees of fineness, the excess of water was appreciably diminished, the process of powdering having opened up some of the larger cavities. Mallet (*Phil. Trans.*, 1880, **171**, 1003), however, attributes a similar loss of water in the case of ammonium alum to the heat generated in crushing the crystals, and the work of Carey Lea (*Phil. Mag.*, 1892, [v], **34**, 46; 1894, [v], **37**, 31) has shown that the enormous mechanical energy which is brought to bear on a substance in powdering is able to bring about the decomposition of substances of far greater stability than crystalline hydrates.

\* Marchwald and Foizik (*Ber.*, 1910, **43**, 1710). In this paper, objection is taken to the method of determination of the atomic weight by heating tellurium dioxide with sulphur, the loss of sulphur dioxide being measured. The authors state that sulphur trioxide is formed as well as the dioxide. This assertion seems unlikely, since excess of sulphur and free tellurium are present, but we have thought it worth while to repeat experiments. In two experiments, 6 grams and 8 grams of highly purified tellurium dioxide were mixed with excess of purified sulphur, silver-leaf being packed in the exit tube. The air having been displaced by nitrogen, the mixture was heated and the gas passed through a dilute acid solution of barium chloride which had been previously boiled to remove dissolved oxygen. A guard tube of distilled water was attached to the bulbs of barium chloride solution, and in these circumstances the solution remained perfectly clear in both experiments, showing that no sulphur trioxide was formed. When the solution of barium chloride, saturated with sulphur dioxide, was exposed to the air, precipitation of barium sulphate was observed in ten minutes. The German chemists also found that a temperature of  $290^\circ$  was necessary, whilst one of us and Bennett (*Trans.*, 1907, **91**, 1849) found that it began at  $130^\circ$ . The lower temperature has been confirmed by inserting a thermometer in the heated mixture of sulphur and tellurium dioxide. If the tellurium dioxide has been previously heated to a very high temperature, it is probable that the reaction would require a higher temperature before it began.

Our object was to devise a method by which both occluded water and adhering solvent would be removed without taking away any of the water of crystallisation. In order to do this, a desiccating agent must be found, the vapour tension of which is less than that of the occluded mother liquor, but not less than the tension of the water of crystallisation, and, secondly, crystals must be permeable to water vapour.

A suitable desiccating agent is found in a mixture obtained by partly dehydrating some of the substance to be dried. If such a mixture is placed in a closed space which contains also some of the same hydrated salt with mother liquor, the vapour tension will be always that of the fully hydrated salt, and the mother liquor will evaporate, leaving crystals of definite and constant weight.

The principle of the method was first suggested by Andreæ (*Zeitsch. physikal. Chem.*, 1891, **7**, 241) for the isolation of hydrates of salts. It was used by Walker and Beveridge (Trans., 1907, **91**, 1597) in the preparation of *p*-toluidine monohydrate. While our work was in progress, it was again used by Cumming (Trans., 1910, **97**, 593) in the isolation of the hydrates of sodium carbonate, and also by Guye and Tsakalotos (*J. Chim. Phys.*, 1909, **8**, 3), whose object was the same as ours, namely, the preparation of hydrates in such a condition that they could be used for atomic-weight determinations.

With regard to the permeability of crystals to water vapour, there are two possibilities. If crystals are to be regarded as built up of crystals of molecular dimensions which are not in absolute contact, it is probable that not only water vapour, but other gases may pass through them. On the other hand, if a crystal be made into a partition between an atmosphere which is saturated with water vapour and a dried atmosphere, dehydration may take place at one surface of the crystal, and the dehydrated layer take up water from the next layer. This process being repeated, the net result will be that water will pass through the crystal from the wet to the dried atmosphere, although the crystal may show no signs of the change which has taken place. We incline to the view that the passage of water through crystals takes place in the second way, since we find that, in the cases examined, hydrated crystals are permeable to water vapour, but anhydrous crystals are impermeable. In order to test whether crystals are permeable to gases, as they would be on the first of the above hypotheses, the following experiments were made. A U-shaped tube was bent so that the limbs were close together. On one end of the tube a flat-bottomed open cup was blown, in which a crystal was cemented by paraffin wax. Mercury was introduced into the bend, the tube was

exhausted, and the open end was sealed. The levels of the mercury in the two limbs of the U-tube were observed with a cathetometer. When air-dried crystals were used, it was found that the mercury was depressed in the limb sealed by the crystal, but never to an extent greater than the maximum tension of aqueous vapour at the temperature of the room. A crystal of potassium chlorate (anhydrous), dried over sulphuric acid, showed no depression of the mercury column, while a crystal of barium chloride ( $\text{BaCl}_2 \cdot 2\text{H}_2\text{O}$ ) showed a depression of about 6 mm., equal to the tension of the water of crystallisation of the salt. Hence we see that under the pressure of an atmosphere, air will not pass through the mass of a crystal, and since in some cases water vapour does so, its passage must take place by some such process as that outlined above.

#### *Drying of Telluric Acid.*

Marckwald states that 15 grams of telluric acid, when kept in a vacuum over phosphoric oxide, lost only 0·3 milligram in two months. Since this statement appeared to be at variance with the previous experience of one of us, the point was investigated in the following way.

Ten grams of the recrystallised acid were weighed in a silica dish against a counterpoise dish of the same material. Both were kept in a vacuous desiccator over phosphoric oxide. Weighings were made at frequent intervals over a period of five months. For the first two days a considerable loss in weight was noticed, no doubt due to surface water. There was a continual decrease in the loss of water, but this loss was still going on when the experiment was stopped. The average daily loss for the last month was 0·1 milligram. In order to investigate further if water was still present in the free state, the dried acid was analysed. Portions were weighed in a dried stoppered silica tube, using a similar silica tube as counterpoise. To the first tube was fitted, by very careful grinding, a connexion made of Jena glass, by means of which a current of air, dried by phosphoric oxide, was enabled to sweep through all traces of water into a bulb, which itself was connected by a ground joint to a U-tube containing phosphoric oxide, the bulb and the U-tube being weighed together. It may be noted that the ground connexion between silica and glass is a very satisfactory arrangement when lubricators are, as in this case, inadmissible. The glass expands more than the silica, so that the joint becomes tighter as the temperature rises. The weights are corrected to vacuum standard. The percentage of water calculated ( $\text{Te}=127\cdot50$ ) is 23·546. The calculated total loss is 30·516:

No.	Telluric acid, grains.	Water collected, gram.	Total loss, gram.	Water found, gram.	Total loss, per cent.	water calc. and found, per cent.	Difference of water calc. and found, per cent.	Difference of total per cent.
								water calc.
1.	3.06816	0.72668	0.94048	23.683	30.654	+ 0.187	+ 0.138	
2.	3.25227	0.56974	0.77251	23.653	30.620	+ 0.168	+ 0.101	
3.	3.26298	0.77020	0.99722	23.601	30.562	+ 0.058	+ 0.046	
4.	3.01471	0.71840	0.93019	23.595	30.551	+ 0.035	+ 0.017	
1.	Telluric acid dried for one month over solid potassium hydroxide.							
2.	" " " over phosphoric oxide.							
3.	" " " three months over phosphoric oxide.							
4.	" " " <sup>fix</sup> "							

It will be seen that with these different amounts of drying there is always an excess of water in the crystallised telluric acid, and this excess is sensibly equal to the excess in the total loss of weight on decomposition, assuming the atomic weight of tellurium to be 127.5.\* It is seen also that this excess of water is not removed by exposure of the acid to the drying of phosphoric oxide in a vacuum for six months. It will be seen later that telluric acid crystals are apparently impermeable to water vapour, and hence the excess of water is retained in the interior of the crystals. We have found that crystals containing true water of crystallisation will allow of the passage of water vapour through them, and we are of opinion that these experiments uphold the view suggested by Gutbier, and supported by Marchwald, that the formula of this acid should be written  $\text{H}_2\text{TeO}_6$ , and not  $\text{H}_2\text{TeO}_4 \cdot 2\text{H}_2\text{O}$ . This view is further strengthened by the fact, discovered by Berzelius, that if the substance is dehydrated until it has the composition  $\text{H}_2\text{TeO}_4$ , the white powder thus obtained can be kept in water for some time without re-hydration. We have repeated this experiment, and we find that after six months' keeping in water, less than a quarter has passed into solution.

In order to show the difference of behaviour of telluric acid and that of a substance containing true water of crystallisation, the following experiment was performed. A weighed quantity of recrystallised copper sulphate, which had been dried to constant weight over partly dehydrated copper sulphate, was placed in a vacuum desiccator containing some of the same salt, which was completely dehydrated. The salt was weighed at intervals:

Date.	Weight of salt.	Change.
Aug. 18th .....	3.43590	- 0.00060
Aug. 26th .....	3.43530	- 0.01225
Oct. 11th .....	3.12305	

Thus, crystallised copper sulphate loses its water of crystallisation

\* From the numbers obtained in these experiments, the ratio of  $\text{TeO}_3 : \text{O}$  is obtained: (1) 100 : 10.042; (2) 100 : 10.020; (3) 100 : 10.016; (4) 100 : 10.049, giving a mean result 100 : 10.032, which gives for the atomic weight of tellurium 127.49.

with considerable rapidity when placed in an atmosphere dried by the anhydrous salt, which is not a very powerful dehydrating agent. The hydrated salt, also, was found to lose practically all its water of crystallisation when dried over phosphoric oxide.

*Drying of Hydrated Salts over the same Salts Partly Dehydrated.*

The substances used in the following experiments were carefully purified by recrystallisation, and finally obtained in small crystals by the sudden cooling of a saturated solution. The substances contained either in vessels of silica or in light stoppered weighing bottles of a wide, shallow pattern, were taken while still moist, and left exposed to the desiccating action of the partly dehydrated salt contained in a vacuum desiccator. Weighings were made at regular intervals until no further loss could be detected even after leaving the substance some considerable time. A counterpoise which was always exposed to the same conditions was used in weighing. It was found to be necessary to readmit air very slowly into the vacuum desiccator before weighing, and also to subject the air to some preliminary process of drying by passing it through a sulphuric acid worm, and then through a long tube containing a mixture similar to that in the desiccator. For the drying agent, the commercial substance without any purification was used. The preliminary dehydration was so regulated that some of the unchanged hydrate always remained in the desiccating material. In all the experiments, it was carefully ascertained that the drying mixture had remained efficient throughout; a large quantity was always used, and, furthermore, it was renewed at frequent intervals.

*Barium Chloride.*

The specimen of barium chloride, after careful purification, remained for about six months in a vacuum over partly dehydrated barium chloride (other experiments being then in progress). A portion of this product was then taken and weighed several times in succession, being in the meantime subject to the treatment described in the previous section:

Date	Weight of salt.	Change in Weight.
Jan. 8th ..	3.57008	- 0.00015
,, 9th .....	3.56993	- 0.00004
,, 11th .....	3.56989	- 0.00001
,, 12th .....	3.56992	- 0.00003
,, 13th .....	3.56993	- 0.00000
,, 15th .....	3.56993	

The first loss, which is considerable, may probably be attributed to adsorption of moisture during transference to a weighing bottle.

The percentage of water of crystallisation in this product was found to be 14·772, a result which, whilst agreeing with other determinations, is above the calculated amount, 14·747.

Thus during the long period of drying, the salt not only did not lose any of its water of crystallisation, but still contained an appreciable excess.

We were, however, able to obtain a specimen of barium chloride with the theoretical percentage of water of crystallisation by the following process. The crystallised salt was first completely dehydrated and finely powdered. It was then left in a vacuum in the presence of partly dehydrated sodium sulphate, and kept there as long as it continued to take up water. Then, in order to remove any adsorbed water, it was placed in another desiccator over partly dehydrated barium chloride, and left there until by three weighings in succession, with four days between each weighing, it was ascertained that the substance had reached a constant weight.

1·84103 grams of this product, on drying to constant weight at 250—270°, lost 0·27155 gram. This corresponds with a percentage of 14·750 instead of 14·747 ( $B_a = 137\cdot37$ ).

#### *Copper Sulphate, CuSO<sub>4</sub>.5H<sub>2</sub>O.*

This salt is known to form lower hydrates with vapour tensions lower than that of the pentahydrate. Two specimens of the salt were used, one in small crystals, and the other finely powdered in a mortar, so that it might be seen if the stability of the hydrate was affected by the mechanical breaking of the crystals. On leaving in an atmosphere dried by partly dehydrated copper sulphate, the weighed salts attained constancy of weight in three weeks, and no further change of more than 0·01 milligram was observed during the next eight weeks.

#### *Potash Alum, K<sub>2</sub>SO<sub>4</sub>.Al<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub>.24H<sub>2</sub>O.*

This salt was chosen on account of the large amount of water which it contains, and the high tension of the water vapour. Two portions were taken, one in small crystals, and the other finely powdered. The salts were not subjected to preliminary drying, but on keeping over the partly dehydrated salt, most of the surface water was found to have disappeared in a week's time, and after a month's drying in this way, the change in weight from week to week did not amount to more than 0·01 milligram on 2·5 grams of salt. As this very small change was sometimes positive and sometimes negative, it may be concluded that it represents the error in weighing.

Oxalic acid (C<sub>2</sub>H<sub>2</sub>O<sub>4</sub>.2H<sub>2</sub>O) was treated in a similar way, but its  
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weight showed a progressive diminution throughout the period of drying. The loss in the third month was found to be due to the volatilisation of the acid at the ordinary temperature, feathery crystals being deposited on the edges of the silica dish.

*Permeability of Crystals to Water Vapour.*

In these experiments a very thin glass flask, of about 5 c.c. capacity, was used, which contained phosphoric oxide. The mouth of the flask was expanded into a shallow cup, in which the crystal was cemented with paraffin wax. For weighing, a similar flask, closed by a similar crystal, but not containing phosphoric oxide, was used as a counterpoise. The crystals used were grown for the purpose, and were free from cracks and flaws. After weighing, the two flasks were placed in an atmosphere containing water vapour of less than the maximum tension at the ordinary temperature, so as to avoid the possibility of the condensation of liquid water on the crystals or the glass. Since the flasks were air-tight, the increase of weight of the one containing phosphoric oxide represents the amount of water which had diffused through the crystal. An experiment was first made with a potassium chlorate crystal, which is, of course, anhydrous. The crystal was 0·86 mm. thick. On June 21st, the flask weighed 7·05803 grams, in the following September, 7·05800 grams, showing that water did not pass through the crystal.

A similar experiment with a telluric acid crystal, 1·62 mm. in thickness, gave the following result:

Date.	Weight of flask and crystal, grams.
May 19th .....	1·29842
" 23rd .....	1·29838
Sept. 9th .....	1·29837
Oct. 22nd .....	1·29839

Hence it is evident that water does not pass through this substance.

With a crystal of copper sulphate 1·93 mm. thick there was a gain in weight of the flask containing phosphoric oxide of 0·04421 gram between March 8th and July 5th. The daily increase was comparatively steady, for the first forty days amounting to 0·00034 gram. During the next thirty days the daily increase was 0·00037 gram. Another crystal of copper sulphate, 2·31 mm. thick, gave similar results, although the average daily increase was less, 0·00011 gram.

*Barium Chloride.*

Crystal 2·56 mm. thick.

Date.	Weight, grams.	Total increase, gram.	Days.	Average increase per day, gram.
May 28th.....	11.01774	0.00061	26	0.00002
June 29th .....	11.01835	0.00105	38	0.00003
July 5th .....	11.01879	0.00536	54	0.00010
" 21st.....	11.02810			

*Potassium Ferrocyanide.*

Water passing through in a direction parallel to the principal plane of cleavage.

Crystal 4·13 mm. thick.

I. June 10th .....	11.33188	0.01085	20	0.00054
" 30th .....	11.34273	0.02299	29	0.00079
July 9th .....	11.35487	0.05847	43	0.00136
" 23rd .....	11.39035			

Crystal 4·10 mm. thick.

II. June 9th .....	3.52139	0.00550	21	0.00025
" 30th .....	3.52689	0.01040	30	0.00033
July 9th .....	3.58179	0.02580	44	0.00059
" 23rd .....	3.54719			

*Potassium Ferrocyanide.*

Water passing through at right angles to the principal plane of cleavage.

Crystal 0·74 mm. thick.

Date.	Weight, grams.	Increase, gram.	Days.	Average increase per day, gram.
I. June 9th .....	7.68214	0.00022	12	0.00002
" 21st .....	7.68236	0.00559	28	0.00021
July 7th .....	7.68803	0.04126	44	0.00094
" 23rd .....	7.72310			

Crystal 0·88 mm. thick.

II. June 9th .....	8.66113	0.00140	21	0.00007
" 30th .....	8.66253	0.01297	28	0.00016
July 7th .....	8.67140	0.04721	44	0.00107
" 23rd .....	8.70834			

*Sodium Thiosulphate.*

Crystal 6·6 mm. thick.

June 28th .....	12.72692	0.00765	7	0.00109
" 30th .....	12.73457	0.02974	16	0.00186
July 9th .....	12.75866	0.08847	26	0.00340
" 19th .....	12.81539			

In order to compare more conclusively the behaviour of hydrated and anhydrous crystals, plates of anhydrite ( $\text{CaSO}_4$ ) and gypsum ( $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ ) of the same thickness were mounted in a similar way in the necks of bulbs containing phosphoric oxide. They were exposed with the counterpoise to moist air for three months. The anhydrite bulb showed no increase in weight, whilst that containing gypsum increased by 7 milligrams. The gypsum crystal showed dehydration on the under side, the upper surface being still bright.

The transference of water in the case of hydrated crystals is accompanied by the dehydration of the crystal on the side nearer the phosphoric oxide. The dehydrating action was in all cases confined to the under surface and to that part of it which was not protected by the paraffin wax, so that the sealing of the crystal was in no way interfered with by the dehydration. The mode of transference of water vapour through these crystals is rather difficult to decide, but the following experiment seems to show that the dehydration which takes place is apparently a necessity.

Crystals of sodium sulphate were placed in a flask, which was closed by a crystal of copper sulphate,  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ , and the flask was weighed against another flask also closed by a crystal of copper sulphate, but containing no sodium sulphate. Both flasks were then placed in a desiccator over anhydrous copper sulphate:

Thickness of crystal = 1.28 mm.

Weight on Aug. 9th C + 0.09009 gram  
 , , Oct. 11th C + 0.09008 ,

Hence, although anhydrous copper sulphate can in ordinary circumstances take up water freely from sodium sulphate, yet under the conditions of the above experiment, the sodium sulphate shows no sign of loss of water during a period of two months, which points to the fact that partial dehydration of the crystal must precede the passage of water vapour through it.

These permeability experiments have an important bearing on the question of occluded water. If, as our experiments seem to show, partial dehydration must precede the passage of water vapour through the crystal, then the method of drying over the partly dehydrated salt can have no effect on the occluded water. This is confirmed both by the experiment which shows that partly dehydrated copper sulphate could not take up water from sodium sulphate when the latter was contained in a flask closed by a crystal of copper sulphate, and by the fact that barium chloride,  $\text{BaCl}_2 \cdot 2\text{H}_2\text{O}$ , even after six months' exposure in a vacuum to the action of the partly dehydrated salt, still contained an excess of

water agreeing very well with determinations by Richards and Marignac (*loc. cit.*):

While these experiments were in progress, a paper was published by Guye and Tsakalotos (*J. Chim. Phys.*, 1909, 7, 215), in which a similar method of drying was described. Barium chloride, in quantities of about 2 grams, was dried at 34°5 in the presence of about 40 grams of anhydrous barium chloride, to which a few drops of distilled water had been added. The distilled water was added in order to ensure the presence of the hydrate  $\text{BaCl}_2 \cdot 2\text{H}_2\text{O}$  in the drying agent.

Their results obtained for the ratio  $\text{BaCl}_2 \cdot 2\text{H}_2\text{O} : \text{BaCl}_2$  are very concordant. The mean percentage of water of crystallisation in the residue was found to be 14·6765, which is below the amount (14·747) calculated from the atomic weights given in the international table for 1911. The percentage in our experiments was 14·72.

From the experience gained in the previous experiments, we are inclined to think that the mere sprinkling of a large amount of barium chloride, spread over the bottom of crystallising dishes, with a few drops of distilled water does not ensure the effective presence of the highest hydrate. Under such conditions, we think that the salt must have been slightly dehydrated in the process of drying.

#### *Conclusions.*

1. It is possible to determine the true weight of a salt containing water of crystallisation with the same degree of accuracy as that which is usually attained when weighing other substances.

2. If compounds containing water of crystallisation are of definite composition, then the products of constant weight, which are obtained by exposing moist crystals to the action of the products of their own partial dehydration, cannot contain less than the theoretical quantity of water.

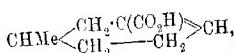
3. Anhydrous crystals will not allow water vapour to pass through them, but salts with water of crystallisation allow this passage with varying degrees of freedom.

4. It is possible to obtain barium chloride with the theoretical percentage of water of crystallisation by re-hydrating the anhydrous salt in the presence of a substance of higher vapour tension. The work is being continued in order to find if this method of obtaining salts with their true amount of water of crystallisation is a general one.

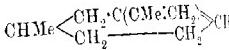
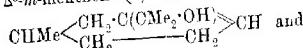
LXI.—*Experiments on the Synthesis of the Terpenes.*  
*Part XVI. Resolution of dl-1-Methyl- $\Delta^3$ -cyclohexene-3-carboxylic Acid and Synthesis of the d- and l-Modifications of  $\Delta^3$ -m-Menthanol(8) and  $\Delta^{3(5)}$ -m-Menthadiene.*

By BERNARD DUNSTAN WILKINSON LUFF (1851 Exhibition Scholar of University College, Nottingham) and WILLIAM HENRY PERKIN, jun.

In a recent communication (*Trans.*, 1910, **97**, 2149, 2151) a method is described by which *dl*-1-methyl- $\Delta^3$ -cyclohexene-3-carboxylic acid:



may be obtained with comparative ease, and the possession of considerable quantities of this acid enabled us to prepare  $\Delta^3$ -m-menthol(8) and  $\Delta^{3(5)}$ -m-menthadiene:



in quantity sufficient to allow of their physical properties being determined with accuracy. During the course of these experiments, it occurred to us that it would be interesting to attempt the resolution of *dl*-1-methyl- $\Delta^3$ -cyclohexene-3-carboxylic acid, and then, with the aid of the active acids, to synthesise and study the physical properties of the corresponding active menthols and menthadienes. With this object in view, we prepared nearly 200 grams of the inactive acid, and instituted a large number of comparative experiments with alkaloids and other active bases, in the hope of discovering some salt by means of which resolution might be easily and rapidly effected. Owing probably to the very feeble acidic properties of the acid, very few of its salts crystallise, and the only salts which we could obtain which were at all suitable for fractional crystallisation were those with brucine and *l*-menthylamine. In our first experiments, we mixed the sodium salt of the acid (1 mol.) with brucine (1 mol.) and the free acid (1 mol.) (compare Pope and Peachey, *Trans.*, 1899, **75**, 1066), and obtained a brucine salt which, when decomposed by sodium carbonate, yielded an acid the rotation of which was only  $[\alpha]_D +5^\circ$ .

The crystalline salt which separates under these conditions is therefore, in the main, the brucine salt of the *d*-acid.

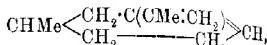
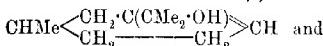
We now treated the acid of  $[\alpha]_D + 5^\circ$  twice again with brucine under the same conditions, and found that the resulting acid had  $[\alpha]_D + 14.5^\circ$ . Further experiments in the same direction produced only a very gradual rise in rotatory power, and it was soon evident that very large quantities of material would be required in order to effect complete resolution in this way.

After a series of experiments with *L*-menthylamine, the course which was ultimately adopted was to obtain, by the brucine process, as much of the acid of rotatory power  $[\alpha]_D + 14.5^\circ$  as possible, and then to continue the resolution with the aid of *L*-menthylamine.

At the same time, a considerable quantity of the *dl*-acid was worked up from the commencement as *L*-menthylamine salt, and the details of these experiments are briefly described in the experimental part of this paper. When the sodium salt of the acid is mixed with *L*-menthylamine hydrochloride, a very sparingly soluble salt is obtained, which, in the main, is the salt of the *d*-acid, but the separation of this salt into its constituents by fractional crystallisation is a most tedious process. The difficulty is apparently of the same kind as that observed in the case of the resolution of *dl*-1-methylcyclonexylidene-4-acetic acid (Perkin, Pope, and Wallach, Trans., 1909, 95, 1794), and to a less extent in the resolution of *dl*-1-methyl- $\Delta^3$ -cyclohexene-3-carboxylic acid (Perkin, Trans., 1910, 97, 2140), and appears to be due to the two constituents of the salt separating from solvents in isomorphous mixtures or mixed crystals. When the *L*-menthylamine salt is crystallised from methyl ethyl ketone, it is easy, in two or three operations, to isolate from the mother liquors small quantities of the levo-acid of the comparatively high rotatory power  $[\alpha]_D - 30^\circ$ , but the separation of the pure salt of the *d*-acid proved to be a very difficult matter, and was only partly possible after a large number of fractional crystallisations carried out under the special conditions described on p. 521. Ultimately, however, after several months' work, we succeeded in isolating, on the one hand, an *L*-menthylamine salt of rotatory power  $[\alpha]_D + 5.9^\circ$ , which yielded, on treatment with sodium carbonate, *d*-1-methyl- $\Delta^3$ -cyclohexene-3-carboxylic acid of rotation  $[\alpha]_D + 40.1^\circ$ . On the other hand, the systematic treatment of the acid,  $[\alpha]_D - 30^\circ$ , with brucine and *L*-menthylamine resulted in the separation of *L*-1-methyl- $\Delta^3$ -cyclohexene-3-carboxylic acid, which was, however, not quite free from the *d*-isomeride, since the highest rotation recorded was  $[\alpha]_D - 35.8^\circ$ .

There is not sufficient evidence that the value  $40.1^\circ$  represents the maximum rotation of the active acids, and, indeed, it is very doubtful whether this is the case (compare p. 527), but we were unable to raise the rotation by further fractional crystallisation.

The difficulty of the separation of the *d*- and *l*-isomerides may be gauged by the fact that, although we started with nearly 200 grams of the externally compensated acid, and every precaution was taken to avoid loss, we were only able to isolate 13 grams of the *d*-acid and 15 grams of the *l*-acid with the rotations given above. These acids were converted into the esters, and then, by the action of magnesium methyl iodide and subsequent elimination of water, into *d*- and *l*- $\Delta^3\text{-}m\text{-menthene}$ (8) and *d*- and *l*- $\Delta^{3:8(9)}\text{-}m\text{-menthadiene}$ :

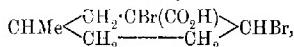


and the observed rotations of the two series may be conveniently tabulated:

	<i>d</i> -Series, [ $\alpha$ ] <sub>D</sub>	<i>l</i> -Series, [ $\alpha$ ] <sub>D</sub>
<i>l</i> -Menthylamine salt.....	+ 5.9°	—
1-Methyl- $\Delta^3$ -cyclohexene-3-carboxylic acid .....	49.1	- 35.8°
Ethyl methylcyclohexenecarboxylate .....	32.5	28.9
$\Delta^3\text{-}m\text{-Menthene}(8)$ .....	20.9	18.5
$\Delta^{3:8(9)}\text{-}m\text{-Menthadiene}$ .....	17.5	12.9

The low values for the menthadienes are probably due to racemisation during their formation from the menthenols by boiling with 5 per cent. oxalic acid. In order to test this, some ethyl *l*-1-methyl- $\Delta^3$ -cyclohexene-3-carboxylate having [ $\alpha$ ]<sub>D</sub> - 23.5° was converted into  $\Delta^3\text{-}m\text{-menthene}(8)$ , and then digested for twelve hours with 10 per cent. oxalic acid. The menthadiene obtained was quite inactive, but no other intramolecular change appeared to have taken place, since this terpene had physical constants almost identical with those of a pure specimen of *d*- $\Delta^{3:8(9)}\text{-}m\text{-menthadiene}$  (Trans., 1910, 97, 2154), namely, b. p. 177—178°/730 mm., and  $n_D$  1.4991.

During the course of this research, some of the *d*-1-methyl- $\Delta^3$ -cyclohexene-3-carboxylic acid of rotation [ $\alpha$ ]<sub>D</sub> + 40.1° was converted into *d*-3:4-dibromo-1-methylcyclohexan-3-carboxylic acid:

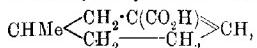


by the action of bromine.

This dibromo-acid was found to melt at 164—165°, and to have [ $\alpha$ ]<sub>D</sub> + 28.5°. The corresponding inactive dibromo-acid melts at 165° (Trans., 1910, 97, 2152).

## EXPERIMENTAL.

*Resolution of dl-1-Methyl- $\Delta^3$ -cyclohexene-3-carboxylic Acid,*



I. *Experiments with Brucine.*—In each experiment, the pure acid (12·5 grams) was suspended in boiling water (750 c.c.), and exactly neutralised with sodium carbonate, a hot concentrated alcoholic solution of the acid (12·5 grams) and brucine (52·5 grams) was then added, and then the whole evaporated on the steam-bath, with frequent additions of small quantities of water, until the alcohol had been removed. During this operation, crystals began to separate, and, on cooling, a large crop of brucine salt was obtained, which was collected, washed with water, and decomposed by sodium carbonate. The crystalline acid was collected, and found to have the following rotation: 0·6395, made up to 20 c.c. with ethyl acetate, gave, in a 2-dm. tube,  $\alpha +0\cdot32^\circ$ , whence  $[\alpha]_D +5\cdot0^\circ$ .

This acid was twice submitted to exactly the same process, and the product then had  $[\alpha]_D +14\cdot5^\circ$ . The mother liquor from the third treatment was acidified, and, after the acid had been distilled in steam, it had  $[\alpha]_D -9\cdot5^\circ$ .

II. *Experiments with l-Menthylamine.\**—When 120 grams of the inactive acid had been resolved to the extent just mentioned, experiments were made with the object of determining whether the separation might not be hastened by using some other active base. After several alkaloids had been tried without success, it was found that the salts with *l*-menthylamine were very sparingly soluble, and crystallised very readily. Unfortunately, owing probably to the formation of isomorphous mixtures, the separation of the isomeric salts proved to be exceedingly tedious, and, as the whole process of separation cannot be given, the following examples will sufficiently illustrate the extent to which separation takes place in the most favourable cases.

(A) The *dl*-acid (10 grams) was dissolved in *N*-sodium hydroxide (70 c.c.) and water (150 c.c.), and, after heating to boiling, a quantity of *l*-menthylamine hydrochloride (7 grams), sufficient to combine with half the acid, was rapidly run in, when the salt separated at once as a crystalline mass, and was collected and dried on porous porcelain. The acid obtained by acidifying the filtrate had a rotation of  $[\alpha]_D -3\cdot4^\circ$ , and, after the menthylamine salt had been twice crystallised from ethyl acetate (in which it is sparingly

\* The *l*-menthylamine hydrochloride used in all these experiments had  $[\alpha]_D -35\cdot4^\circ$ .

soluble in the cold, but readily so on boiling), and decomposed by sodium carbonate, the acid had  $[\alpha]_D + 9.0^\circ$

(B) A specimen of the acid, which had  $[\alpha]_D + 9.5^\circ$  (60 grams), was dissolved in *N*-sodium hydroxide (420 c.c.), and mixed with excess of *l*-menthylamine hydrochloride (90 grams). The salt which separated was collected, dried on porous porcelain, and crystallised three times from ethyl acetate, when it exhibited the following rotation:

0.7117, made up to 20 c.c. with ethyl alcohol, gave, in a 2-dcm. tube,  $\alpha - 1.28^\circ$ , whence  $[\alpha]_D - 18^\circ$ .

The mother liquor was evaporated to a small bulk, and the salt, which separated on cooling, was collected, and the filtrate decomposed with sodium carbonate, when a small quantity of acid (5 grams) was obtained, which, after steam distillation, had  $[\alpha]_D - 10^\circ$ . A considerable quantity of the acid of  $[\alpha]_D - 10^\circ$  which had accumulated (60 grams) was dissolved in *N*-sodium hydroxide (420 c.c.), treated with excess of *l*-menthylamine hydrochloride (90 grams), and the salt recrystallised from the least possible quantity of methyl.ethyl ketone. After collection the filtrate yielded, on treatment with sodium carbonate and steam distillation in the usual way, 4 grams of an acid, which had  $[\alpha]_D - 30^\circ$ .

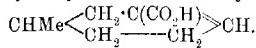
(C) The acid of rotation  $[\alpha]_D + 14.5^\circ$ , which had been obtained as the result of the partial resolution with brucine, was dissolved, in quantities of 16 grams, in *N*-sodium hydroxide (112 c.c.), and mixed with *l*-menthylamine hydrochloride (25 grams). The salt was collected, dissolved in boiling methyl ethyl ketone, and, when the whole had cooled to  $40^\circ$ , the crystalline mass was rapidly collected. After this operation had been repeated six times, 8 grams of the *l*-menthylamine salt of the *d*-acid resulted: 0.6012, made up to 20 c.c. with alcohol, gave, in a 2-dcm. tube,  $\alpha + 0.36^\circ$ , whence  $[\alpha]_D + 5.9^\circ$ .

On further recrystallisation, the rotation of this salt did not alter; it is therefore possibly free from the salt of the *l*-acid.

As has already been stated, it is a comparatively easy matter to isolate small quantities of the *l*-acid of rotation  $[\alpha]_D - 30^\circ$  (see *b*), but the purification of the salt of the *d*-acid is always very tedious. The best way of effecting this seems to be to dissolve the salt in a considerable quantity of a boiling mixture of 90 parts of methyl ethyl ketone and 10 parts of alcohol, and then to shake well in a corked flask until the whole has cooled to  $45^\circ$ , and filter rapidly by the aid of the pump. This process is repeated with the crop of crystals which separates from the mother liquor until the bulk of the *l*-salt has been removed. The large quantities of mother liquor which will have accumulated are then concentrated considerably,

and, after the salt has crystallised out, the filtrate is decomposed with sodium carbonate, and the crude, rather brown *l*-acid purified by distillation in steam. By repeating these processes many times, separation of the *d*- and *l*-isomerides is ultimately accomplished.

*d*-1-Methyl- $\Delta^3$ -cyclohexene-3-carboxylic Acid,



The *l*-menthylamine salt of this acid, obtained as described on p. 522, has  $[\alpha]_D + 5.9^\circ$ , melts at about  $150-152^\circ$ , and is readily soluble in alcohol and in boiling ethyl acetate or methyl ethyl ketone, but very sparingly so in these two solvents in the cold. The acid, obtained from the salt by decomposition with sodium carbonate, was distilled in steam and left in contact with porous porcelain until dry; it then melted at  $62-64^\circ$  (the *dl*-acid melts at  $58^\circ$ ):

0.1164 gave 0.2928 CO<sub>2</sub> and 0.0914 H<sub>2</sub>O. C=68.7; H=8.7.

C<sub>8</sub>H<sub>12</sub>O<sub>2</sub> requires C=68.6; H=8.6 per cent.

0.5218, made up to 20 c.c. with ethyl acetate, gave, in a 2-dcm. tube,  $\alpha + 2.09^\circ$ , whence  $[\alpha]_D + 40.1^\circ$ .

*Ethyl d*-1-Methyl- $\Delta^3$ -cyclohexene-3-carboxylate.—This ester was prepared by digesting the acid (12 grams) with 100 c.c. of 10 per cent. alcoholic sulphuric acid for two hours on the steam-bath; the product was then diluted with water, and extracted with ether.

The ethereal solution was thoroughly washed with dilute sodium carbonate, dried, evaporated, and the ester distilled, when it passed over constantly at  $150-151^\circ/100$  mm. 0.6148, made up to 20 c.c. with ethyl acetate, gave, in a 2-dcm. tube,  $\alpha + 2.0^\circ$ , whence  $[\alpha]_D + 32.5^\circ$ .

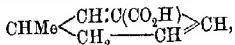
*d*-3: 4-Dibromo-1-methylcyclohexan-3-carboxylic Acid (compare p. 520).—In preparing this dibromo-acid, the pure *d*-acid (1 gram), dissolved in chloroform (5 c.c.) and cooled to  $-10^\circ$ , was mixed with a slight excess of bromine (1.2 grams), and, after remaining in the freezing mixture for one hour, it was kept at the ordinary temperature for two hours, during which a quantity of solid separated. The chloroform was allowed to evaporate, the residue left in contact with porous porcelain until quite dry, and then recrystallised from formic acid, in which it is sparingly soluble, and from which it separates in colourless leaflets, melting at  $165^\circ$ , at which temperature the *dl*-dibromo-acid also melts:

0.2848 gave 0.3567 AgBr. Br=53.2.

C<sub>8</sub>H<sub>12</sub>O<sub>2</sub>Br<sub>2</sub> requires Br=53.3 per cent.

0.6202, made up to 20 c.c. with ethyl acetate, gave, in a 2-dcm. tube,  $\alpha + 1.77^\circ$ , whence  $[\alpha]_D + 28.5^\circ$ .

A curious result was obtained in an attempt to study what change in optical activity would result if the dihydro-acid:



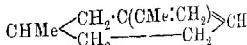
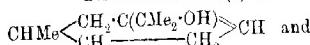
could be prepared from the active dibromo-acid by the elimination of two molecules of hydrogen bromide. A considerable quantity (14 grams) of an acid which had  $[\alpha]_D + 17.4^\circ$  was converted into the ester; this was dissolved in pure ether, cooled to  $-10^\circ$ , and mixed with the quantity of bromine calculated for the formation of the dibromo-additive compound, a quantity which was rapidly absorbed.

The ether was then distilled off under slightly diminished pressure, and the residue added to a concentrated and boiling solution of potassium hydroxide (30 grams) in methyl alcohol, when a vigorous action took place and potassium bromide was immediately precipitated. The product, diluted with water, was nearly neutralised with hydrochloric acid, evaporated, and mixed with excess of acid, when a syrup separated, which soon crystallised. The acid was collected, washed, and separated into four portions by fractional distillation in steam, but in each case, after collecting and draining on porous porcelain, the acid melted at  $60-62^\circ$ , and consisted of 1-methyl- $\Delta^3$ -cyclohexene-3-carboxylic acid, since when mixed with this acid, there was no alteration in melting point. The identity was also confirmed by analysis. (Found, C = 68.5; H = 8.8. Calc., C = 68.6; H = 8.8 per cent.)

The different portions of the acid were mixed, and the rotation determined.

1.1197, made up to 20 c.c. with ethyl acetate, gave, in a 2-dm. tube,  $a + 1.95^\circ$ , whence  $[\alpha]_D + 17.4^\circ$ , and therefore no change in rotation had occurred during the course of the above somewhat drastic experiments. Since almost the whole of the acid was recovered, it is obvious that when ethyl 3:4-dibromo-1-methylcyclohexan-3-carboxylate is digested with methyl-alcoholic potassium hydroxide, the alkali acts simply as an agent for removing bromine.

*d- $\Delta^3$ -m-Menthanol(8) and  $\Delta^{3:8(9)}$ -m-Menthadiene,*



The synthesis of *d- $\Delta^3$ -m-menthanol(8)* was carried out by adding ethyl *d*-1-methyl- $\Delta^3$ -cyclohexene-3-carboxylate (12 grams) to an ethereal solution of magnesium methyl iodide prepared from 6 grams of magnesium, and, after remaining overnight, the product was decomposed by water and distilled in steam. The distillate was

extracted with ether, the ethereal solution dried and fractionated, when *d*- $\Delta^3$ -*m*-menthenol(8) passed over constantly at 107—108°/25 mm. as a viscid syrup, which exhibited the following properties: *d* 20/20° 0·9235, *n*<sub>D</sub> 1·4791, M 47·3 (calc., 47·16). 0·7231, made up to 20 c.c. with ethyl acetate, gave, in a 2-dcm. tube,  $\alpha + 1\cdot 51^\circ$ , whence  $[\alpha]_D + 20\cdot 9^\circ$ .

These properties agree closely with those of *dl*- $\Delta^3$ -*m*-menthenol(8) (Trans., 1910, 97, 2158), which has b. p. 102°/14 mm., *d* 20/20° 0·9268, *n*<sub>D</sub> 1·4798.

In order to obtain  $\Delta^{3,8(9)}$ -*m*-menthadiene, the menthenol was digested for four hours with 5 per cent. oxalic acid, and the product distilled in steam. After extraction with ether, and distillation first alone, and then twice over sodium, the terpene distilled constantly at 179°/730 mm., and had *n*<sub>D</sub> 1·4972, whereas *dl*- $\Delta^{3,8(9)}$ -*m*-menthadiene (*loc. cit.*, p. 2154) distilled at 181—182°/760 mm., and had *n*<sub>D</sub> 1·4975.

0·7117, made up to 20 c.c. with ethyl acetate, gave, in a 2-dcm. tube,  $\alpha + 1\cdot 25^\circ$ , whence  $[\alpha]_D + 17\cdot 5^\circ$ .

*l*-1-*Methyl*- $\Delta^3$ -cyclohexene-3-carboxylic Acid, *l*- $\Delta^3$ -*m*-Menthenol(8), and *l*- $\Delta^{3,8(9)}$ -*m*-Menthadiene.

In experiment (C) on p. 522, a method is described by which *l*-1-methyl- $\Delta^3$ -cyclohexene-3-carboxylic acid may be comparatively easily obtained with the rotation  $[\alpha]_D - 30^\circ$ , and, when a considerable quantity of this acid had accumulated, it was again converted into the *l*-menthylamine salt, and, after a long series of fractional crystallisations, an acid (15 grams) was obtained, which exhibited the following rotation: 0·7447, made up to 20 c.c. with ethyl acetate, gave, in a 2-dcm. tube,  $\alpha - 2\cdot 67^\circ$ , whence  $[\alpha]_D - 35\cdot 8^\circ$ . No doubt, if this acid had again been converted into the *l*-menthylamine salt, and the fractional crystallisation continued, an acid of somewhat higher rotation would have been obtained, but the loss which this must have entailed would have been serious.

*Ethyl l*-1-*methyl*- $\Delta^3$ -cyclohexene-3-carboxylate, prepared from the acid by means of alcoholic sulphuric acid, exactly as described in the case of the corresponding *d*-ester (p. 523), distilled at 148—150°/100 mm. 0·8239, made up to 20 c.c. with ethyl acetate, gave, in a 2-dcm. tube,  $\alpha - 2\cdot 38^\circ$ , whence  $[\alpha]_D - 28\cdot 9^\circ$ .

*l*- $\Delta^3$ -*m*-Menthenol(8) was obtained from this ester (11 grams) by treatment with magnesium methyl iodide ( $Mg = 5$  grams) in the usual way, and, after distillation in steam, distilled constantly at 102—103°/14 mm. 0·8111, made up to 20 c.c. with ethyl acetate, gave, in a 2-dcm. tube,  $\alpha - 1\cdot 50^\circ$ , whence  $[\alpha]_D - 18\cdot 5^\circ$ . This menthenol was digested with 5 per cent. oxalic acid for two hours,

and, after distillation in steam, and then three times over sodium, *l*- $\Delta^{3:8(9)}$ -*m*-menthadiene boiled constantly at 181–182°/760 mm. 0·8118, made up 20 c.c. with ethyl acetate, gave, in a 2-dm. tube,  $\alpha - 1\cdot05^\circ$ , whence  $[\alpha]_D - 12\cdot9^\circ$ .

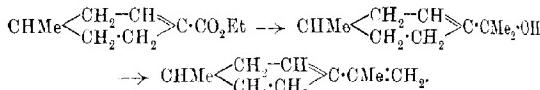
The determination of the refractive index gave  $n_D$  1·4969.

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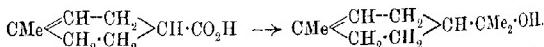
LXII.—*Experiments on the Synthesis of the Terpenes.*  
*Part XVII.* *d*- $\Delta^3$ -*p*-Menthanol(8) and *d*- $\Delta^{3:8(9)}$ -*p*-Menthadiene.

By TSAN QUO CHOU and WILLIAM HENRY PERKIN, jun.

THE externally compensated modifications of  $\Delta^3$ -*p*-mentheno(8) and  $\Delta^{3:8(9)}$ -*p*-menthadiene were first prepared in 1905 (Perkin and Pickles, Trans., 87, 647) from the ester of *dl*-1-methyl- $\Delta^3$ -cyclohexene-4-carboxylic acid by treatment with magnesium methyl iodide and subsequent elimination of water:



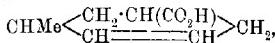
Shortly afterwards, Kay and Perkin (Trans., 1906, 89, 833) resolved *dl*-1-methyl- $\Delta^3$ -cyclohexene-4-carboxylic acid by means of the brucine salt into the *d*- and *l*-acids, which were obtained with rotations  $[\alpha]_D + 101\cdot1^\circ$  and  $-100\cdot8^\circ$  respectively. From these active acids the *d*- and *l*-modifications of  $\Delta^3$ -*p*-mentheno(8) and  $\Delta^{3:8(9)}$ -*p*-menthadiene were prepared, and the rotations of all these substances are tabulated on p. 529. During the progress of these experiments on the synthesis of the terpenes, other attempts were made to prepare active menthenols and menthadienes by processes similar to that just mentioned. Thus, in 1908, Fisher and Perkin (Trans., 93, 1871) resolved *dl*-1-methyl- $\Delta^1$ -cyclohexene-4-carboxylic acid into the *d*- and *l*-acids of rotations  $[\alpha]_D + 50^\circ$  and  $-52^\circ$  respectively, and prepared from these the *d*- and *l*-modifications of terpineol which were obtained with the rotations  $[\alpha]_D + 44\cdot2^\circ$  and  $-46\cdot6^\circ$ :



The attempt to convert these active terpineols into the pure active

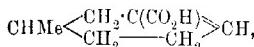
limonenes was not successful, since, even when the elimination of water was carried out at the ordinary temperature with the aid of magnesium methyl iodide, the resulting limonene had a rotation of only  $5^\circ$ .

Shortly afterwards (Perkin, Trans., 1910, **97**, 2131), the resolution of *dl*-1-methyl- $\Delta^5$ -cyclohexene-3-carboxylic acid:



was attempted with the aid of *l*-menthylamine as the active base, and the *d*- and *l*-acids were obtained with the rotations  $[\alpha]_D + 33.1^\circ$  and  $-30.9^\circ$  respectively. These yielded, on treatment with magnesium methyl iodide and subsequent elimination of water,  $\Delta^5$ -*m*-mentheno(8) and  $\Delta^{5,8(9)}$ -*m*-menthadiene, which, in the *d*-series, had  $[\alpha]_D + 36.7^\circ$  and  $+29.6^\circ$  respectively.

In the paper directly preceding the present communication (p. 521), experiments on the resolution of *dl*-1-methyl- $\Delta^5$ -cyclohexene-3-carboxylic acid:



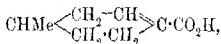
are described, and it is there shown that this acid may be resolved with the aid of *l*-menthylamine into the *d*- and *l*-modifications with the rotations  $[\alpha]_D + 40.1^\circ$  and  $-35.8^\circ$  respectively, and these were converted, by the usual methods, into the corresponding *d*- and *l*-menthols and menthadienes, of which the highest rotations observed, in the *d*-series, were  $[\alpha]_D + 20.9^\circ$  and  $+17.5^\circ$  respectively. In all these cases, separation of the optically active acids from the externally compensated modifications has always been a long and tedious process, and there appears to be no doubt that this is largely, if not wholly, due to the isomeric salts separating from solvents as isomorphous mixtures or mixed crystals, which are only very gradually resolvable by further fractional crystallisation. This difficulty might conceivably be got over if the active base employed for the separation could be varied, but the cyclohexenecarboxylic acids are, unfortunately, so feebly acidic that very few of their salts with active bases are sufficiently stable or well characterised to make them suitable for fractional crystallisation.

When the available data are carefully considered, it is difficult to avoid the conclusion that, in the cases detailed above, separation may have, after all, been incomplete. The salts of the active acids were probably still partly racemic, and in the form of mixed crystals, and, for these reasons, separation by further fractional crystallisation was practically impossible, at all events with the comparatively small amounts of material which were available.

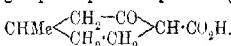
Confirmatory evidence of this is afforded by the experiments of

Fisher and Perkin on the resolution of *d*-1-methyl- $\Delta^1$ -cyclohexene-3-carboxylic acid (see p. 526). The value observed for the *t*-acid was  $[\alpha]_D - 52^\circ$ , and that this is probably not the maximum value is indicated by the fact that the *t*-terpineol obtained from this acid had only  $[\alpha]_D - 46.6^\circ$ , whereas an *t*-terpineol has been obtained from pinene with  $[\alpha]_D - 117.5^\circ$  (Ertschikowsky, *Ber.*, 1896, 29, 887).

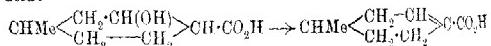
Considerations such as these made it desirable that the actual extent of the resolution effected by the fractional crystallisation of the salts of the cyclohexene acids with active bases should, at least in one instance, be experimentally tested, and we have therefore carried out an interesting series of experiments in connexion with the optical activity of 1-methyl- $\Delta^3$ -cyclohexene-4-carboxylic acid:



which have a direct bearing on this problem. In a communication recently published (Gardner, Perkin, and Watson, *Trans.*, 1910, 97, 1759, 1767), it was shown that *d*-1-methylcyclohexan-3-one (from pulegone,  $[\alpha]_D + 8.8^\circ$ ) is converted, by the action of sodamide and carbon dioxide, into a carboxylic acid, in which it was assumed that the carboxyl group occupied the position (4):



That this acid, which has  $[\alpha]_D + 97.2^\circ$ , is, in fact, *d*-1-methylcyclohexan-3-one-4-carboxylic acid has now been proved in the following way. When this keto-acid is reduced with sodium amalgam, it is converted into *d*-1-methylcyclohexan-3-ol-4-carboxylic acid, which has  $[\alpha]_D - 31.8^\circ$ , and this, on treatment with sulphuric acid at 85—90°, yields *p*-toluic acid, a proof that the carboxylic group in the hexanol acid occupies the position (4) in relation to the methyl group. The elimination of water from *d*-1-methylcyclohexan-3-ol-4-carboxylic acid takes place with difficulty, but it may be accomplished (p. 533) with the aid of phosphorus trichloride, and the resulting *d*-1-methyl- $\Delta^3$ -cyclohexene-4-carboxylic acid:



was found to have  $[\alpha]_D + 150.1^\circ$ . This acid was converted into the corresponding *d*- $\Delta^3$ -*p*-menthenol(8) and  $\Delta^{3:8(9)}$ -*p*-menthadiene by the usual methods, and the  $[\alpha]_D$  values observed (I) may be conveniently tabulated in comparison with those previously observed by Kay and Perkin (II) (*loc. cit.*):

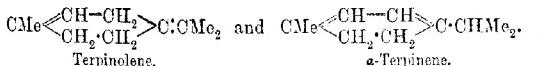
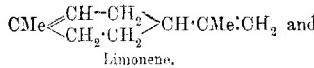
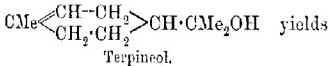
	I.	II.
d-L-Methyl- $\Delta^3$ -cyclohexene-4-carboxylic acid .....	+150.1°	+101.1°
Ethyl d-L-methylcyclohexenecarboxylate .....	122.3	86.5
d- $\Delta^3$ -p-Menthanol(8).....	83.2	67.3
d- $\Delta^{3,5(9)}$ -p-Menthadiene.....	100.0	98.2

This table shows quite clearly that the substances obtained by Kay and Perkin had rotations which were only about two-thirds of the maximum value. There is, however, one curious exception to this, and that is the case of the menthadienes, which, although derived from menthenols of the widely different values as  $[\alpha]_D + 83.2^\circ$  and  $+67.3^\circ$ , had, in both cases, practically the same rotations, namely,  $+100.0^\circ$  and  $+98.2^\circ$ . This seems to indicate quite clearly that some racemisation must have taken place in any case during the formation of the menthadiene from the menthol of rotation  $[\alpha]_D + 83.2^\circ$ .

That racemisation does undoubtedly take place under certain conditions, to some extent at least, is proved by the following experiment.

Pure d- $\Delta^3$ -p-menthanol(8) of rotation  $[\alpha]_D + 83.2^\circ$  was converted into d- $\Delta^{3,5(9)}$ -p-menthadiene by two different processes, namely, (i) by digesting with 5 per cent. oxalic acid, and (ii) by the action of magnesium methyl iodide in the cold. The menthadiene obtained in (i) had  $[\alpha]_D + 100.0^\circ$ , whereas the preparation resulting from (ii) had a rotation of  $[\alpha]_D + 90.4^\circ$  only. Racemisation in unsaturated compounds is usually assumed to be due to the reversible migration of the double linking, with consequent loss of optical activity, and seems to have been observed previously only in cases where the double linking is closely associated with the asymmetric carbon atom.

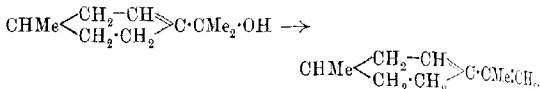
Thus, for example, Wallach has shown that terpineol yields, on treatment with dehydrating agents, not only limonene, but also terpinolene and  $\alpha$ -terpinene:



This group of terpenes probably represents an equilibrium mixture, but, however that may be, it is quite clear that, if the terpineol in the first instance is optically active, the reversible change into terpinolene alone must ultimately result in the inactivity of the

whole. This migration of the double linking with consequent loss of optical activity accounts therefore in a satisfactory manner for the fact that Fisher and Perkin (*loc. cit.*) were unable to obtain an active limonene with a rotation of more than  $5^\circ$  (*d*-limonene has  $[\alpha]_D + 105^\circ$ ) from active terpineol by the elimination of water.

It is, however, difficult to understand how this explanation of loss of activity can be applied to the case of racemisation during the elimination of water from *d*- $\Delta^3$ -*p*-menthenol(8):

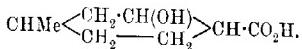
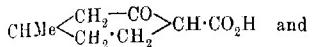


since migration of the double linking could hardly affect the asymmetric grouping  $>\text{CHMe}$  to which optical activity is due unless, indeed, some profound change in constitution is assumed to take place.

Moreover, it is clear that a profound change in constitution does not take place, because the menthadiene obtained is found to exhibit all those physical properties which are known to be associated with the presence of the conjugated double linking.

*Note by W. H. Perkin.*—The paper by Kay and Perkin already referred to (Trans., 1906, **89**, 850; compare *ibid.*, 1905, **87**, 639) contains a description of some of the physical properties of *dl*- $\Delta^3$ - $\Delta^5$ (*9*)-*p*-menthadiene, which subsequent investigation has shown to be incorrect, and which has resulted in some confusion (compare Perkin and Wallach, Trans., 1910, **97**, 1437). As this terpene was very carefully prepared from crystalline *d*- $\Delta^3$ -*p*-menthenol(8), and had the correct boiling point (184–185°), it was difficult to understand the inaccuracy of the density and refraction values. The reason has now been ascertained to be the following one. The terpene was obtained in rather small quantity, and was washed into the bottle with a little ether and sent to Sudbury for investigation, the intention being that the final distillation should be carried out just before the physical constants were determined. This was, however, not done, and the determinations were made with the specimen in the condition in which it was received. The specimen has now been re-examined, and, after twice distilling over sodium, it gave the following correct values: b. p. 184–185°; *d* 20/20° 0.8598;  $n_D$  1.4919; M 45.9. Calc. for  $C_{10}H_{16}F^2$  45.24.

*d*-1-Methylcyclohexan-3-one-4-carboxylic Acid and *d*-1-Methylcyclohexan-3-ol-4-carboxylic Acid,



*d*-1-Methylcyclohexan-3-one-4-carboxylic acid had already been prepared in small quantities by Gardner, Perkin, and Watson (Trans., 1910, **97**, 1767) from *d*-1-methylcyclohexan-3-one (from pulegone) by the action of sodamide and carbon dioxide at the ordinary temperature on its solution in light petroleum, but the yield obtained at that time was very unsatisfactory. As it was necessary to obtain a large quantity of this acid for the experiments described in the present communication, we made a number of comparative experiments, and succeeded in working out the following method of preparation, which gives excellent results. *d*-1-Methylcyclohexan-3-one (from Schimmel,  $[\alpha]_D +8.8^\circ$ ), in quantities of 100 grams, is dissolved in one and a-quarter litres of light petroleum (b. p. 50—60°) in a three-necked flask fitted with a reflux condenser and mechanical stirrer, and the whole heated to boiling on the steam-bath. The steam is then turned off, the stirrer set in motion, and powdered sodamide (40 grams) added in several portions during twenty minutes, when a rapid evolution of ammonia takes place. A rapid current of carefully dried carbon dioxide is now passed, when reaction readily occurs with sufficient rise of temperature to keep the light petroleum boiling, and, in a short time, a quantity of the sodium salt of the ketonic acid separates. As soon as the liquid ceases to boil, the steam is turned on again, and the passage of the carbon dioxide continued for three and a-half hours; the contents of the flask are allowed to cool, and washed into a separating funnel with sufficient ice water to dissolve all the sodium salt. The aqueous layer is separated, filtered, if necessary, and acidified with ice-cold dilute hydrochloric acid, when the ketonic acid separates as a crystalline mass, which is collected and drained on porous porcelain. The yield of air-dry acid is usually about 70 grams, but on more than one occasion 90 grams have been obtained; in this condition it is pure enough for conversion into the hydroxy-acid (see below). The pure keto-acid is obtained from this product by dissolving in ether, extracting with sodium carbonate, and cautiously adding dilute hydrochloric acid to the alkaline solution until traces of yellow impurity have been precipitated. After filtering, the filtrate deposits, on acidifying, pure *d*-1-methylcyclohexan-3-one-4-carboxylic acid as a colourless, crystalline mass. The petroleum layer,

separated from the sodium salt of the acid in the manner described above, yields, on evaporation, a good deal of unchanged ketone, which is readily purified by distillation in steam.

*d-1-Methylcyclohexan-3-ol-4-carboxylic Acid.*—In preparing this acid, *d*-1-methylcyclohexan-3-one-4-carboxylic acid (15 grams) is dissolved in sodium carbonate, diluted to one litre with hot water (50°), and reduced in a wide-necked bottle with one kilo. of freshly prepared sodium amalgam (3 per cent.), which is added all at once.

During the operation, which takes about three hours, a rapid current of carbon dioxide is passed, the whole is vigorously stirred by a mechanical stirrer, and the temperature gradually raised to 70° by circulating a stream of hot water round the bottle. After remaining overnight, the aqueous liquor is decanted from the mercury, acidified with hydrochloric acid, and distilled in steam.

By this means, unchanged keto-acid, which is always present, is decomposed, the ketone passes over and is recovered from the distillate. The liquid in the steam distillation flask is evaporated on the steam-bath until a pale yellow oil commences to separate; it is then saturated with salt, and extracted three times with ether.

After drying over anhydrous sodium sulphate, and evaporating, the ethereal solution deposits a viscous syrup, which gradually becomes semi-solid; it distils at 135—190°/22 mm., but with some decomposition, and the distillate has  $[\alpha]_D$  about  $-7.5^\circ$  (compare p. 528). This doubtless consists of a mixture of the *cis*- and *trans*-modifications of *d*-1-methylcyclohexan-3-ol-4-carboxylic acid.

The best way to purify this hydroxy-acid is with the aid of its ethyl ester, which is readily prepared by digesting on the steam-bath with a large excess of 10 per cent. alcoholic sulphuric acid for two to three hours. The ester is isolated by diluting with water and extracting with ether in the usual manner, the ethereal solution washed with sodium carbonate, dried, evaporated, and the residue fractionated, when almost the whole quantity passes over at 135°/20 mm.:

0.1679 gave 0.3961 CO<sub>2</sub> and 0.1484 H<sub>2</sub>O. C=64.4; H=9.8.

C<sub>10</sub>H<sub>16</sub>O<sub>3</sub> requires C=64.5; H=9.7 per cent.

*d* 20/20° 1.026; n<sub>D</sub> 1.458; M 49.25 (calc., 49.51). 1.0221, made up to 20 c.c., with ethyl acetate, gave, in a 2-dm. tube,  $\alpha +0.6^\circ$ , whence  $[\alpha]_D +5.9^\circ$ .

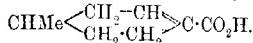
*Conversion of d-1-Methylcyclohexan-3-ol-4-carboxylic Acid into p-Toluic Acid.*—The hydroxy-acid employed in this experiment was the crystalline modification obtained by leaving the semi-solid mixture direct from the reduction of the keto-acid in contact with porous porcelain. This acid dissolves readily in concentrated sulphuric acid, and, when the colourless solution is heated at

85—90°, evolution of sulphur dioxide occurs freely with very little darkening.

After a few minutes, the hot solution is diluted with water, the crystalline precipitate collected, washed well, dissolved in dilute sodium carbonate, and digested with animal charcoal. Finally the acid is again precipitated and crystallised from dilute acetic acid. (Found, C=70·5; H=6·0. Calc., C=70·6; H=5·9 per cent.)

This acid separated from dilute acetic acid in colourless, glistening needles, melted at 177—178°, and had all the properties of *p*-toluic acid. The identity was further proved by mixing it with a specimen of pure *p*-toluic acid, when there was no alteration in the melting point.

*d,l-Methyl- $\Delta^3$ -cyclohexene-4-carboxylic Acid,*



The conversion of *d,l-methylcyclohexan-3-ol-4-carboxylic acid* into *d,l-methyl- $\Delta^3$ -cyclohexene-4-carboxylic acid* by the elimination of water does not take place very readily, but digesting the hydroxy-acid with acetyl chloride containing phosphorus trichloride, and distilling the product first under diminished pressure and then in steam, yields small quantities of the unsaturated acid. Other dehydrating agents give a similar result, but the best yield is apparently produced under the following conditions. Ethyl *d,l-methylcyclohexan-3-ol-4-carboxylate*, in quantities of 10 grams, is digested on the water-bath with an equal weight of phosphorus trichloride for one hour, and then heated to boiling on the sand-bath for half an hour.

The orange-coloured product is poured into excess of alcohol, and, after two hours, water is added, the ester extracted with ether, the ethereal solution washed with sodium carbonate, dried, evaporated, and the residue distilled, when crude ethyl *d,l-methyl- $\Delta^3$ -cyclohexene-4-carboxylate* passes over at 148—150°/100 mm., the yield being about 60 to 70 per cent. of that theoretically possible. The ester is hydrolysed by digesting with excess of methyl-alcoholic potassium hydroxide, and, after diluting with water, evaporating until free from methyl alcohol and acidifying, the semi-solid precipitate is collected and distilled in a current of steam. The unsaturated acid passes over with some difficulty, but in a pure condition, and is collected and left in contact with porous porcelain until dry. From the aqueous filtrate, a further considerable quantity of acid is recovered by neutralising, evaporating to a small bulk, and acidifying:

0·1101 gave 0·2760 CO<sub>2</sub> and 0·0849 H<sub>2</sub>O. H=68·5; H=8·6.

C<sub>8</sub>H<sub>12</sub>O<sub>2</sub> requires C=68·6; H=8·6 per cent.

1·007, made up to 20 c.c. with ethyl acetate, gave, in a 2-dcm. tube,  $\alpha + 15\cdot02^\circ$ , whence  $[\alpha]_D + 150\cdot1^\circ$ . *d*-1-*Methyl*- $\Delta^3$ -cyclohexene-4-carboxylic acid is very sparingly soluble in water, but the hot concentrated solution deposits the acid as a chalky powder, which under the microscope, is seen to consist of well-defined, elongated, four-sided prisms. It melts at 136—137° (the *dl*-acid melts at 134°: Trans., 1905, 87, 646), and the solution in sodium carbonate reduces permanganate instantly.

*Ethyl d*-1-*Methyl*- $\Delta^3$ -cyclohexene-4-carboxylate.—The ester obtained by the action of phosphorus trichloride on ethyl *d*-1-methylcyclohexan-3-ol-4-carboxylate (see above) is far from pure, and usually has a rotation of  $[\alpha]_D + 65^\circ$  only; the pure ester is obtained from the pure acid by means of alcohol and sulphuric acid, but esterification takes place with some difficulty, especially in the cold. The acid (18 grams) was left in contact with alcohol (200 c.c.) and sulphuric acid (15 c.c.) for twenty-four hours, and then heated for three hours on the steam-bath. After adding water, the ester was extracted with ether, the ethereal solution washed with sodium carbonate (which extracted 3 grams of unchanged acid), dried, evaporated, and the ester distilled, when it passed over constantly at 151—152°/100 mm.:

0·1094 gave 0·2870 CO<sub>2</sub> and 0·0954 H<sub>2</sub>O. C=71·5; H=9·7.

C<sub>10</sub>H<sub>16</sub>O<sub>2</sub> requires C=71·4; H=9·5 per cent.

*d* 20/20° 0·9757; n<sub>D</sub> 1·4688; M 47·9 (calc., 47·3). 0·9639, made up to 20 c.c. with ethyl acetate, gave, in a 2-dcm. tube,  $\alpha + 11\cdot79^\circ$ , whence  $[\alpha]_D + 122\cdot3^\circ$ .

*d*-3-*Bromo*-1-*methyl*cyclohexan-4-carboxylic Acid.\*—In order to prepare this acid, *d*-1-methyl- $\Delta^3$ -cyclohexene-4-carboxylic acid was mixed with a large excess of fuming hydrobromic acid (saturated at 0°), in which it gradually dissolved, and, after remaining overnight, the product was heated at 80° for one hour and then mixed with three volumes of water. The bromo-acid, which separated as a voluminous, crystalline mass, was collected, washed, and crystallised from formic acid, from which it was deposited, on slow cooling, as a mass of asbestos-like threads, melting at 133—134°:

0·1633 gave 0·1395 AgBr. Br=36·4.

C<sub>8</sub>H<sub>13</sub>O<sub>2</sub>Br requires Br=36·2 per cent.

1·1866, made up to 20 c.c. with ethyl acetate, gave, in a 2-dcm. tube,  $\alpha + 8\cdot50^\circ$ , whence  $[\alpha]_D + 71\cdot7^\circ$ . This bromo-acid dissolves readily in sodium carbonate, and when the solution was boiled, a small quantity of an oil having the odour of a bromo-

\* The corresponding *dl*-bromo-acid has already been described (Trans., 1905, 87, 646), but the melting point was accidentally omitted. It softens at 135° and melts at 140—142°.

hydrocarbon separated, and, after this had been removed, the alkaline solution gave, on acidifying, a colourless precipitate of *d*-1-methyl- $\Delta^3$ -cyclohexene-4-carboxylic acid, which melted at 134–136°, and had approximately the same rotation,  $[\alpha]_D + 150^\circ$ , as before the conversion into the bromo-acid.

*d*-3: 4-Dibromo-1-methylcyclohexan-4-carboxylic Acid.—This dibromo-acid is readily obtained when *d*-1-methyl- $\Delta^3$ -cyclohexene-4-carboxylic acid, dissolved in chloroform and cooled to –10°, is mixed with a chloroform solution of the calculated amount of bromine. Addition takes place slowly in the cold, but if the temperature of the solution is allowed to gradually rise to 17°, the colour of the bromine disappears, and the chloroform solution deposits, on evaporation in the air, a solid residue. After remaining in contact with porous porcelain until dry, the substance was crystallised from formic acid, from which it separated as a colourless, glistening mass of flat needles, melting at about 138°:

0·1591 gave 1·1990 AgBr. Br = 53·1.

$C_8H_{12}O_2Br_2$  requires Br = 53·3 per cent.

0·9364, made up to 20 c.c. with ethyl acetate, gave, in a 2-dcm. tube,  $\alpha + 9·58^\circ$ , whence  $[\alpha]_D + 102·2^\circ$ . This dibromo-acid dissolves readily in sodium carbonate, but the solution, on boiling, does not deposit a bromo-hydrocarbon, as has so often been observed in analogous cases.

*Reduction of d*-1-Methyl- $\Delta^3$ -cyclohexene-4-carboxylic Acid. Formation of the cis- and trans Modifications of 1-Methylcyclohexan-4-carboxylic Acid.

The reduction of *d*-1-methyl- $\Delta^3$ -cyclohexene-4-carboxylic acid was carried out with colloidal palladium and hydrogen according to the excellent method described by A. Skita (*Ber.*, 1909, **42**, 1630), with the modification that the process was conducted at the ordinary pressure instead of under a pressure of two atmospheres. Gum arabic (5 c.c. of a solution of 25 grams in 100 c.c. of water) was diluted with warm water (200 c.c.), mixed with a solution of the unsaturated acid (15 grams) in alcohol (200 c.c.), and, after cooling to 25°, a solution of palladous chloride (1 gram) in water was added. The solution was transferred to a long, narrow cylinder, and hydrogen passed in for two days; the product was then distilled in steam, when an oil passed over at first, but towards the end of the distillation this crystallised.

The distillate was neutralised with sodium carbonate, evaporated to about 300 c.c. and mixed with powdered ice and a few c.c. of permanganate solution, and allowed to remain for one hour, but

hardly any decoloration of the permanganate took place, showing that reduction was practically complete. After removing the excess of permanganate with sodium sulphite, the acid was liberated by hydrochloric acid and again distilled in steam. The distillate was extracted with ether, the ethereal solution dried, evaporated, and the residual oil fractionated, when almost the whole passed over at 141°/20 mm. as a colourless oil, which, in the ice chest, deposited a quantity of crystals. The product was transferred to porous porcelain, and, when the oil had been absorbed, the residue (2 grams) was crystallised from a little formic acid; it consisted then of pure *trans-1-methylcyclohexan-4-carboxylic acid*:

0·1154 gave 0·2853 CO<sub>2</sub> and 0·1031 H<sub>2</sub>O. C=67·4; H=9·9.  
C<sub>8</sub>H<sub>14</sub>O<sub>2</sub> requires C=67·6; H=9·8 per cent.

This acid melted at 112°, and is obviously identical with the hexahydro-*p-toluic acid* described by Perkin and Pickles (Trans., 1905, **87**, 644). The *p-toluidide* was prepared by warming the acid (1 gram) with phosphorous trichloride (0·5 gram) on the water-bath, and then mixing with an ethereal solution of *p-toluidine* (5 grams). The ethereal solution was washed with water, dried, and evaporated, during which operation the *p-toluidide*, which is rather sparingly soluble in ether, separated in crystals. It is readily soluble in alcohol, and separates from 80 per cent. alcohol as a glistening mass of flat prisms, which melt at 179--180°:

0·1482 gave 8·4 c.c. N<sub>2</sub> at 17° and 735 mm. N=6·3.  
C<sub>15</sub>H<sub>21</sub>ON requires N=6·1 per cent.

The porous plates used in the purification of the *trans*-acid were extracted with ether in a Soxhlet apparatus, and the oily acid boiled with much water and freshly precipitated calcium carbonate.

When the filtered solution was concentrated on the water-bath a calcium salt separated in long needles; this was found to be the calcium salt of the *trans*-acid, and, on acidifying, 0·7 gram of this acid separated at once in the crystalline form. On further concentration, the mother-liquors of this calcium salt deposited a second crop, which consisted principally of the salt of the *cis*-acid, and when this and a further crop had been removed, the filtrate yielded, on acidifying, an oily acid which distilled constantly at 140°/20 mm.

After the purification of the calcium salt had been repeated, the *cis-1-methylcyclohexan-4-carboxylic acid* was analysed:

0·1149 gave 0·2827 CO<sub>2</sub> and 0·1034 H<sub>2</sub>O. C=67·2; H=10·0.  
C<sub>8</sub>H<sub>14</sub>O<sub>2</sub> requires C=67·6; H=9·8 per cent.

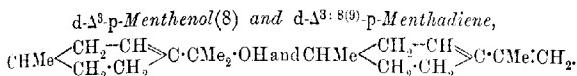
The *p-toluidide* of this acid was prepared in the way already described in the case of the *trans*-acid. It is more soluble in ether or alcohol than the *p-toluidide* of the *trans*-acid, and separates

from 70 per cent. alcohol in colourless needles, which soften at 135° and melt at 142—143°:

0·1833 gave 10·3 c.c. N<sub>2</sub> at 15° and 736 mm. N=6·4.

C<sub>15</sub>H<sub>21</sub>ON requires N=6·1 per cent.

So far as could be judged, the product of the reduction of *d*-1-methyl-Δ<sup>3</sup>-cyclohexene-4-carboxylic acid, under the conditions described above, consists of about 75 per cent. of the *cis*- and 25 per cent. of the *trans*-acids.



In order to prepare the former of these substances, pure ethyl *d*-1-methyl-Δ<sup>3</sup>-cyclohexene-4-carboxylate (20 grams) was added to an ethereal solution of magnesium methyl iodide (containing 9 grams of magnesium), and, after remaining for twenty-four hours, water was added and the product distilled in steam. The ethereal extract of the distillate was dried, evaporated, and the residue distilled, when almost the whole quantity passed over at 105°/20 mm.:

0·1414 gave 0·4028 CO<sub>2</sub> and 0·1502 H<sub>2</sub>O. C=77·7; H=11·8.

C<sub>10</sub>H<sub>18</sub>O requires C=77·9; H=11·7 per cent.

*d* 20/20° 0·9236; n<sub>D</sub> 1·4783; M 47·2 (calc., 47·2). 0·9099, made up to 20 c.c. with ethyl acetate, gave, in a 2-dem. tube,  $\alpha + 7\cdot57^\circ$ , whence  $[\alpha]_D + 83\cdot2^\circ$ . *d*-Δ<sup>3</sup>-p-Menthanol(8) is a colourless, rather viscid oil, which, even on long keeping in the ice chest, showed no signs of crystallising; it possesses a pungent odour, recalling that of peppermint and cymene.

*d*-Δ<sup>3</sup>:8(9)-p-Menthadiene was first prepared by boiling the pure menthol (15 grams) with 200 c.c. of 5 per cent. oxalic acid in a reflux apparatus for ten hours with frequent shaking, when elimination of water was practically complete. The product was distilled in steam, the distillate extracted with ether, the ethereal solution dried, evaporated, and the terpene distilled twice alone and then three times over sodium, when it boiled constantly at 184—185°/776 mm.:

0·1296 gave 0·4183 CO<sub>2</sub> and 0·1356 H<sub>2</sub>O. C=88·0; H=11·7.

C<sub>10</sub>H<sub>16</sub> requires C=88·2; H=11·8 per cent.

The amount available for the density determination was so small that the value obtained must be accepted as approximate only.

*d* 16/16° 0·8649; n<sub>D</sub> 1·4965; M 45·9; calc. for C<sub>10</sub>H<sub>16</sub> F<sup>2</sup> 45·24. 0·8544, made up to 20 c.c. with ethyl acetate, gave, in a 2-dem. tube,  $\alpha + 8\cdot54^\circ$ , whence  $[\alpha]_D + 100\cdot0^\circ$ . For reasons stated in the intro-

duction to this paper (p. 529), it seemed probable that racemisation had taken place to some extent during the formation of this terpene from *d*-Δ<sup>3</sup>-*p*-menthenol(8) under the conditions just described, and that the value  $[\alpha]_D + 100^\circ$  does not represent the maximum rotation of the terpene. In order to test this supposition, the following experiment was carried out. Pure ethyl *d*-1-methyl-Δ<sup>3</sup>-cyclohexene-4-carboxylate (12 grams) was added to magnesium methyl iodide (containing 7 grams of magnesium), and, after remaining overnight and then warming on the steam-bath for one hour, the product was mixed with water and dilute hydrochloric acid and distilled in steam (compare footnote, Trans., 1910, **97**, 2154). The ethereal extract of the distillate was dried, evaporated, and the residue, which distilled almost completely below  $85^\circ/20$  mm., three times fractionated over sodium.

The *d*-Δ<sup>3</sup>, 8(9)-*p*-menthadiene thus obtained distilled constantly at  $182-183^\circ/760$  mm., and had an even lower rotation than the preparation made by the first process. 0·8410, made up to 20 c.c. with ethyl acetate, gave, in a 2-dm. tube,  $\alpha + 7\cdot6^\circ$ , whence  $[\alpha]_D + 90\cdot4^\circ$ .

The authors wish to state that much of the heavy expense of this investigation was met by a grant from the Research Fund of the Royal Society.

THE UNIVERSITY,  
MANCHESTER.

LXIII.—*The Optical Properties of Compounds Containing an Asymmetric "Quaternary" Carbon Atom. Part I. The Synthesis of β-Phenyl-β-methylvaleric Acid and of αs-Methylethylsuccinic Acid.*

By JOHN KENNETH HAROLD INGLIS.

ALTHOUGH it has been known for many years that an optically active compound often loses its activity on keeping, or on treatment with certain reagents, yet very little has been discovered in regard to the mechanism by which such changes take place. Now, in most optically active compounds hitherto investigated, one of the four groups of the asymmetric grouping is a hydrogen atom or a halogen atom, or a hydroxyl group. If the asymmetric group-

ing contained only groups which were less reactive than these, we should expect it to be correspondingly more stable as regards racemisation; and it therefore seemed that the study of the asymmetric "quaternary" carbon atom might throw some light on the mechanism underlying these changes. An increased stability for such a class of compound is shown in the case of the camphoric acids. Here, of the two asymmetric carbon atoms, one is tertiary and the other quaternary. When an active form of camphoric acid is heated, only one of these groupings undergoes racemisation, the quaternary grouping being unchanged. Thus *d*-camphoric acid, on heating, gives some *l*-isocamphoric acid, and, similarly, *l*-camphoric acid gives some *d*-isocamphoric acid. The complete racemisation of *d*- or *l*-camphoric acid does not appear to take place. The behaviour of such a substance therefore showed that the study of compounds which owed their whole activity to an asymmetric quaternary carbon atom might be profitable.

The first type of compound investigated was one in which the four groups of the asymmetric grouping were an acid group and three hydrocarbon radicles. An acid group was necessary to ensure the substance being easily resolved by means of alkaloids. It was necessary also to have a crystalline substance, in order that it might be easily purified. An acid containing a carbon atom linked to the four groups methyl, ethyl, phenyl, and  $\text{CH}_2\text{CO}_2\text{H}$ , was therefore prepared by the following series of reactions. Acetophenone was treated with magnesium ethyl bromide, and the tertiary alcohol isolated. This alcohol, on treatment with hydrogen chloride, gave the corresponding chloride, which, however, could not be purified by distillation, and was therefore used in the crude state. The crude chloride, on treatment with sodium malonic ester, gave a small yield of a derivative of malonic ester, from which, after saponification, the corresponding acid could be obtained. This acid could be purified by recrystallisation, and, on heating, lost carbon dioxide and gave the required acid.

This acid, however, has shown itself unsuited for further experiment. It is a liquid at the ordinary temperature, and does not even form well-crystallising salts, except with quinine. The brucine salt, for example, could only be obtained as an oil. Fractional crystallisation, however, of the quinine salt did not appear to give a resolution of the acid. An equally unsatisfactory result was obtained with the closely-related acid containing a propyl group in place of the ethyl. A small quantity of this acid was prepared, but it also seemed to be a liquid. It was, therefore, not more closely studied.

As these monobasic acids had thus shown themselves unsuited

for the experiments in view, an investigation has been made of an acid of a somewhat different type. *αs*-Methylethylsuccinic acid has already been prepared in several ways, and shown to be a crystalline solid melting at 104°. The most convenient method of preparation seemed to be that due to Higson and Thorpe (Trans., 1906, 89, 1467). According to these authors, if the sodium derivative of cyanoacetic ester suspended in alcohol is treated with the cyanohydrin of methyl ethyl ketone, an 80 per cent. yield is obtained of ethyl  $\alpha\beta$ -dicyano- $\beta$ -methyl- $\beta$ -ethylpropionate (ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylvalerate), an oil boiling at 162°/20 mm. This oil, on hydrolysis, gives a good yield of methylethylsuccinic acid. I have employed their method of preparation on several occasions, but have been unable to obtain a better yield than 40 per cent. The oil obtained boiled at 165°/19.5 mm., and on analysis proved to be pure. In Higson and Thorpe's experiments, the product, judging from the results of the analysis, must have been far from pure.

*αs*-Methylethylsuccinic acid is readily soluble in water, and forms crystalline salts with brucine and quinine. The quinine salt, on fractional crystallisation, can be separated into two fractions, from which the active forms of the acid may be obtained. The brucine salt, on the other hand, is very easily soluble in water, and fractional crystallisation did not apparently effect a resolution.

#### *Preparation of Phenylmethylethylcarbinol.*

This alcohol was first obtained by Klages (Ber., 1902, 35, 3506) in the preparation of a styrene by the action of magnesium ethyl iodide on acetophenone. He did not, however, obtain the substance in a very pure state. The following process was found to give a satisfactory result: 24.4 grams of magnesium (1 atom) were dissolved in a mixture of about 110 grams of ethyl bromide (1 mol.) and 500 c.c. of dry ether. When all the magnesium had dissolved, the solution was cooled, and a solution of 115 grams of acetophenone (1 mol.) in 500 c.c. of dry ether was added slowly, the mixture being well shaken and the temperature kept below 10°. When all had been added, the mixture was left to remain in ice for 1½ hours. Excess of ice and hydrochloric acid were then added slowly. The ethereal solution was separated, washed well with aqueous sodium hydroxide, and then kept over solid potassium hydroxide. The dry ethereal solution was then distilled, and, after the ether had been removed, the distillation was continued under 20 mm. pressure, most of the liquid then passing over at 107—112°. It was found that if every trace of acid was not removed, the alcohol decomposed, even on distillation under diminished pressure, into olefine and

water. A small amount of decomposition took place, even when there was no acid present; but distillation under a lower pressure gave, finally, a nearly pure specimen, boiling at 106·5–108·5°/15 mm. (Found, C=79·8; H=9·37. Calc., C=80·0; H=9·3 per cent.)

*Preparation of Phenylmethylethylcarbinyl Chloride.*

This substance was also prepared by Klages (*loc cit.*) by the action of hydrogen chloride on the alcohol. It was found to decompose on distillation, even in a vacuum. The crude chloride, therefore, diluted with ether, was washed free from acid, and, after drying, the ether was removed by distillation in a vacuum up to 40°. The bromide was also prepared, but was no more stable. The percentage of halogen was estimated by boiling with dilute nitric acid and an excess of standard silver nitrate, the excess of silver being determined by means of thiocyanate. The purest specimen of the chloride contained Cl=19·6, whereas  $C_{10}H_{13}Cl$  requires Cl=21·1 per cent. The purest specimen of the bromide contained Br=34·6; Calc., Br=37·5 per cent.

*Condensation of the Chloride with Sodiomalonic Ester.*

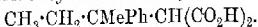
This reaction was carried out under various conditions, but in no case was a good yield of condensation product obtained. Most of the chloride was converted into the olefine, and only a small portion condensed with the malonic ester. The following procedure gave the best yield: 4·6 grams of sodium were dissolved in 50 c.c. of alcohol, and 36 grams (a slight excess) of malonic ester added. This mixture was cooled to the ordinary temperature, and an amount of crude chloride, containing 33 grams of pure chloride, was added. The mixture was left for twenty hours, and then heated on the water-bath for four hours. The alcohol was then distilled off, water added, the oil was extracted with ether, and the ethereal solution dried. After removal of the ether, the distillation was continued under diminished pressure, most of the liquid boiling at 95–105°/25–30 mm.; but a small fraction remained in the flask, and finally boiled at 190–200°/25 mm. The weight of this fraction was 4–5 grams. Several portions of this substance obtained in this way were mixed and redistilled, when the boiling point was 182–187°/16 mm. This oil was not analysed, but was immediately saponified by heating with 40 per cent. potassium hydroxide and a little alcohol on the water-bath. In about one hour the saponification was complete, and from the liquid after dilution with water and acidifying with hydrochloric

acid, an acid was extracted which dissolved easily in warm water, but separated as an oil on cooling. This oil became crystalline after some time, and after repeated crystallisation melted at 134·5–136°:

0·1762 gave 0·4288 CO<sub>2</sub> and 0·1124 H<sub>2</sub>O. C=66·36; H=7·10.  
0·0892 (silver salt) gave 0·0428 Ag. Equiv. of acid=118.

C<sub>15</sub>H<sub>16</sub>O<sub>4</sub> requires C=66·1; H=6·78 per cent. Equiv.=118.

It is evident, therefore, that the condensation product was the ester of  $\alpha$ -phenyl-sec.-butylmalonic acid,



In the above condensation the bulk of the substance was recovered as a liquid boiling at 95–105°/25–30 mm. This consisted of a mixture of malonic ester and the olefine, CH<sub>3</sub>·CH·CMePh, prepared by Klages (*loc. cit.*). This olefine, on treatment with hydrobromic acid, yielded an oil, which, on condensing with sodium malonic ester and subsequent treatment as before, gave further quantities of apparently the same acid; for the two substances melted at almost exactly the same temperature as a mixture of them. Hence we may conclude that the olefine combines with hydrogen bromide to give the same bromide as would be obtained from the alcohol.

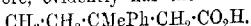
#### *Preparation of $\beta$ -Phenyl- $\beta$ -methylvaleric Acid.*

The malonic acid derivative, on being heated, began to lose carbon dioxide at a temperature slightly above its melting point. There remained an oil which showed at the ordinary temperature no signs of crystallisation. On cooling a solution in dry ether crystals were formed, but could not be isolated. They appeared to melt below 0°. The acid was distilled under diminished pressure, and boiled at 174°/14 mm. The sodium salt was prepared, but did not crystallise from water. It was readily soluble in alcohol, but could not be recovered from it in a pure crystalline form. The silver salt was therefore prepared and analysed:

0·2173 gave 0·0780 Ag. Ag=35·9.  
0·2257 „ 0·3983 CO<sub>2</sub>, 0·1042 H<sub>2</sub>O, and 0·0812 Ag. C=48·1;  
H=5·1; Ag=36·0.

C<sub>15</sub>H<sub>15</sub>O<sub>2</sub>Ag requires C=48·2; H=5·0; Ag=36·1 per cent.

The acid, therefore, evidently has the formula



#### *Attempted Resolution of the Acid.*

When the acid was dissolved in sodium hydroxide, the excess of alkali neutralised with hydrochloric acid, and a solution of

quinine hydrochloride added, a gummy precipitate was formed, which rapidly became solid. This was collected, and found to be sparingly soluble in boiling water, and to crystallise out on cooling. It was, however, very readily soluble in absolute alcohol, and was recrystallised by adding small quantities of water to a concentrated alcoholic solution. The salt melted at 86—88°, and was repeatedly crystallised from aqueous alcohol in order to effect a resolution. The various fractions, however, had approximately the same melting point and specific rotation, showing that no resolution had taken place.

*Synthesis of  $\alpha$ -Phenyl- $\alpha$ -methylbutylmalonic Acid.*

Phenylmethylpropylcarbinol was prepared by Klages (*Ber.*, 1902, 35, 2643) by the action of magnesium propyl iodide on acetophenone. Under the action of hydrogen chloride it gives the chloride, which, like the other chlorides of this type, decomposes on distillation. Fifteen grams of this chloride were prepared and condensed with sodiomalonic ester. The mixture was left overnight, and then heated for six hours on the water-bath. The alcohol having been distilled off, water was added. The oil which separated was extracted with ether, and washed and dried as usual. After removal of the ether, the residual oil was distilled under 12 mm. pressure, and most of it passed over below 110°, only a small fraction remaining when the temperature reached 150°. This residual oil was then hydrolysed with 40 per cent. aqueous potassium hydroxide, and thus yielded about 0·7 gram of an acid, which could be crystallised from water, and then melted at 124—126°:

0·1910 gave 0·4654 CO<sub>2</sub> and 0·1311 H<sub>2</sub>O. M = 7·6; C = 66·4.

C<sub>14</sub>H<sub>18</sub>O<sub>4</sub> requires C = 67·2; H = 7·2 per cent.

The acid was evidently not pure, but from its synthesis and analysis had the constitution CH<sub>3</sub>·CH<sub>2</sub>·CH<sub>2</sub>·CMePh·Cl(CO<sub>2</sub>H)<sub>2</sub>. As on heating it to expel carbon dioxide a liquid acid resulted, a closer examination of it was not made.

*Condensation of Methyl Ethyl Ketonecyanohydrin and Sodiocyanooacetic Ester.*

The cyanohydrin was prepared according to the method given by Ultee (*Rec. trav. chim.*, 1909, 28, 1), and 25 grams of it were condensed with the sodium derivative of cyanoacetic ester according to Higson and Thorpe's directions (*loc. cit.*). After twelve hours, water was added, the liquid acidified, and extracted with ether. The ethereal solution was washed with dilute sodium carbonate and again with water, and then dried over calcium chloride. The ether having been distilled off, the residue was dis-

tilled under diminished pressure, a lower fraction, consisting mainly of cyanoacetic ester, and a higher fraction, boiling at 140—170°/20 mm., being thus obtained. This fraction of high boiling point consisted mainly of impure ethyl  $\alpha\beta$ -dicyano $\beta$ -methylvalerate, and weighed 17—18 grams, the yield thus being about 36 per cent. This yield was hardly improved by using the method employed by Higson and Thorpe in the case of acetoncyanohydrin, namely, using excess of ethyl cyanoacetate, and adding the sodium derivative to an alcoholic solution of the cyanohydrin. Similarly, there was no improvement in the yield when the reaction was carried out below 0°.

The liquid boiling at 140—170°/20 mm. was redistilled, and then boiled at 164—166°/19·5 mm.:

0·2287 gave 0·5158 CO<sub>2</sub> and 0·1498 H<sub>2</sub>O. C=61·5; H=7·26.

C<sub>10</sub>H<sub>14</sub>O<sub>2</sub>N<sub>2</sub> requires C=61·8; H=7·2 per cent.

The hydrolysis of this compound to *as*-methylethylsuccinic acid was effected by the method described by Higson and Thorpe, and was almost quantitative. The acid, after crystallisation from water, melted sharply at 104°.

#### *The Resolution of as-Methylethylsuccinic Acid.*

Experiments have been made with both the quinine and brucine salts of the acid, but only the former seems to make a resolution possible. In the case of the brucine salt which is very soluble in water, two fractions were obtained of different melting point; but they had approximately the same specific rotation, and each fraction yielded the inactive acid. The quinine salt can be crystallised from water, in which it is only moderately soluble, and the less soluble fractions gave an acid which was dextrorotatory. As, however, only small quantities of the active acid have been obtained, and it was not free from the racemic form of the acid, no details as regards specific rotation can be given.

Further experiments are being made on the resolution of the acid, and when the active forms have been obtained in the pure state, the racemisation phenomena will be studied.

UNIVERSITY COLLEGE,  
READING.

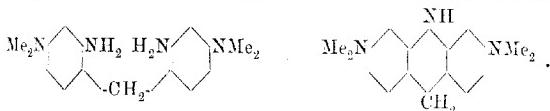
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LXIV.—*Fluorone Derivatives.*

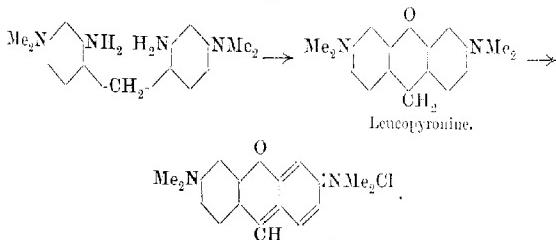
By FRANK GEORGE POPE and HUBERT HOWARD.

In our last communication (Trans., 1910, **97**, 1023) we described certain derivatives of phenylfluorone, and gave reasons for preferring the para-quinonoid structure of such substances, rather than the ortho-quinonoid form advocated by Kehrmann. We have now obtained other derivatives of phenylfluorone and phenylluorime, and are able to give, as it seems to us, other arguments against the ortho-quinonoid formulation of such compounds.

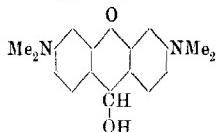
The first fluorime to be prepared was Pyronine-G, or tetramethyl-aminofluorime, which was obtained by Bender (D.R.-P. 59003), whilst its constitution was settled by Biehringer (*J. pr. Chem.*, 1896, [ii], **54**, 232), who prepared it by the oxidation of the product formed on condensation of formaldehyde and dimethyl-*m*-amino-phenol. The constitution of this compound was deduced in the following manner. The tetramethyldiaminodiphenylmethane formed by the condensation of formaldehyde and dimethyl-*m*-amino-phenol was nitrated, and the nitro-groups were then reduced to amino-groups. The resulting amino-compound, by elimination of ammonia, was converted into a dihydroacridine, which must consequently be represented as being produced in the following manner:



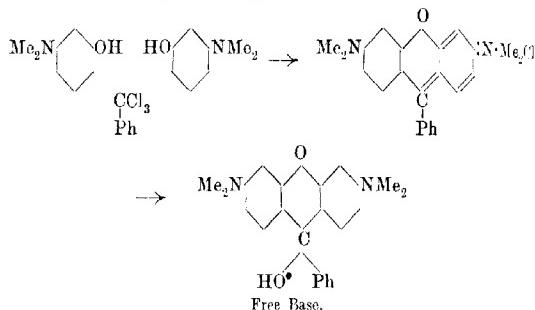
When the tetramethyldiaminodiphenylmethane was diazotised and the solution boiled, leucopyronine was produced, and this oxidised readily in acid solution to form pyronine salts. From this method of formation it was considered that the substances obtained possessed a para-quinonoid configuration:



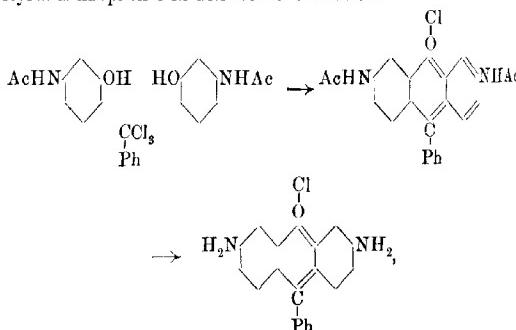
Similar substances have been obtained by Möhlau and Koenig (*Ber.*, 1894, **27**, 2895), and it has been shown that on treatment with alkali hydroxide they yield  $\psi$ -bases of the type:



The rosamine bases are derivatives of phenylfluorone, a tetramethylrosamine (3:6-tetramethyldiamino-9-phenylxanthene chloride) being obtained by Heunmann from the action of benzotrifluoride on dimethyl-*m*-aminophenol in benzene solution:

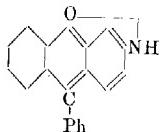


whilst Kehrmann (*Ber.*, 1908, **41**, 3440) prepared the simplest member of the series by the action of benzotrifluoride on mono-acetyl-*m*-aminophenol in nitrobenzene solution:

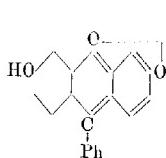


and gave to it the ortho-quinonoid structure, chiefly by reason of the analogy between rosamines and *apo*-safranone. On diazotisation

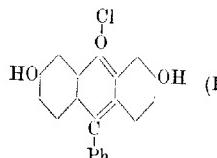
in acid solution he obtained from it hydroxyphenylfluorone, and he also showed that on treatment with alkali hydroxide it yielded an unstable  $\phi$ -base which rapidly lost water, and was converted into an anhydro-base, to which he assigned the following structure:



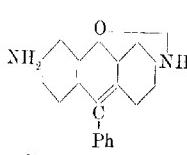
It certainly seems strange that he should here use the oxonium type in preference to the ammonium type of structure, since the basic properties of nitrogen are definite, whilst the existence of oxonium salts is not at present universally accepted. Again, if Kehrmann's oxonium structure is correct, one would expect that rosamine chloride should be similar to hydroxyphenylfluorone hydrochloride and to the dichloroxanthonium chloride obtained by us:



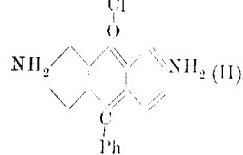
Hydroxyphenylfluorone (Kehrmann).



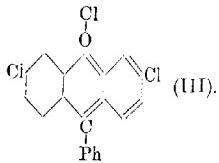
Hydroxyphenylfluorone hydrochloride.



Rosamine anhydro-base (Kehrmann).



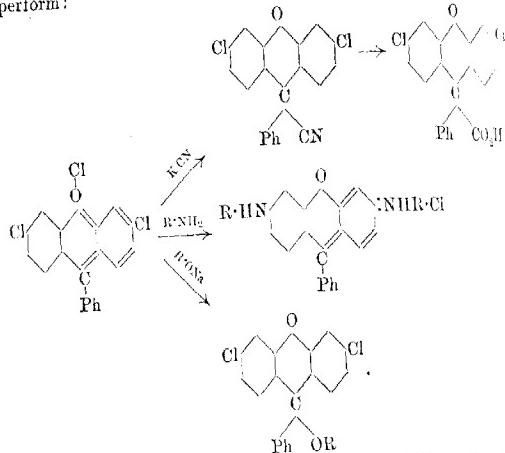
Rosamine chloride.



Dichlorophenylxanthonium chloride.

The three compounds (I, II, III) being all oxonium salts, would show similar behaviour, since the nucleus substituent groups hardly exert any influence. In reality, we find that phenyl-

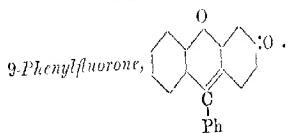
fluorone hydrochloride is readily hydrolysed in aqueous solution, rosamine chloride is the chloride of a strong base, and that dichloro-xanthonium chloride is extremely reactive, as is shown by the following scheme of transformations which we have been able to perform:



Consequently it seems to us, taking these facts into consideration, that an ortho-quinonoid configuration for the fluorones is untenable.

It may be objected that our formation of compounds of the rosamine type from the xanthonium chloride is an argument in favour of the ortho-quinonoid formation, but it should be pointed out that a change of structure, with shifting of the "oxonium" chlorine atom, must occur, since in the formation of nitriles, acids, and ethers even the most staunch supporter of the oxonium structure would hardly attach cyano-, carboxy-, and alkoxy-groups to the quadrivalent oxygen atom.

## EXPERIMENTAL.



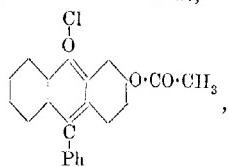
Two grams of anhydrous zinc chloride were heated with 2.16 grams of dihydroxybenzhydrol and 0.94 gram of phenol for

four hours to 160°. The fusion was extracted with hot water, dissolved in sodium hydroxide solution (in presence of zinc dust), the solution filtered, and the resulting hydroxyxanthen precipitated by dilute acetic acid. It was then collected, well washed with water, and redissolved in dilute sodium hydroxide solution. A stream of air was then drawn through the liquid for some days, when a precipitate of the fluorone was gradually produced. The precipitate was collected, washed, dried, and recrystallised from alcohol:

0·1118 gave 0·3428 CO<sub>2</sub> and 0·0452 H<sub>2</sub>O. C=83·63; H=4·49.  
C<sub>19</sub>H<sub>12</sub>O<sub>2</sub> requires C=83·82; H=4·41 per cent.

*9-Phenylfluorone* separates from alcohol in brown scales, which possess a green reflex. It is quite insoluble in aqueous alkaline hydroxides, and even in dilute solutions of the mineral acids. It is soluble in concentrated sulphuric acid, the solution being dark brown in colour. From this solution it may be reprecipitated by the addition of water, as an orange powder. It melts at 200°, is soluble in hot alcohol, chloroform, or pyridine, but insoluble in light petroleum.

*3-Acetoxy-9-phenylxanthonium chloride,*

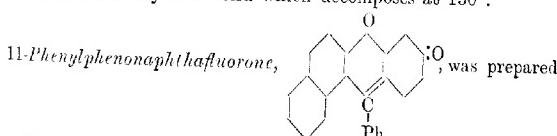


was obtained by dissolving 2·72 grams of phenylfluorone in chloroform and adding 0·78 gram of acetyl chloride to the liquid. The solution was poured into light petroleum, the yellow precipitate collected, washed with light petroleum, and dried in a vacuum:

0·0916 gave 0·240 CO<sub>2</sub> and 0·0332 H<sub>2</sub>O. C=71·46; H=4·03.  
0·1060 „ 0·0440 AgCl. Cl=10·27.

C<sub>21</sub>H<sub>13</sub>O<sub>3</sub>Cl requires C=71·89; H=4·28; Cl=10·13 per cent.

The chloride is a yellow solid which decomposes at 130°.

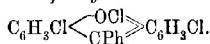


from the corresponding xanthen by drawing a stream of air through its alkaline solution. The precipitate was collected, well washed, and recrystallised from alcohol:

0·1100 gave 0·3450 CO<sub>2</sub> and 0·0436 H<sub>2</sub>O. C=85·54; H=4·49.  
C<sub>23</sub>H<sub>14</sub>O<sub>2</sub> requires C=85·71; H=4·35 per cent.

It separates from alcohol in brown scales, possessing a green reflex, and melts at 237°.

*3:6-Dichloro-9-phenylxanthonium Chloride,*

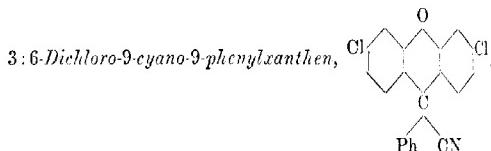


Five grams of hydroxyphenylfluorone were dissolved in 20 grams of phosphoryl chloride, and 10 grams of phosphorus pentachloride were then added. The blood-red liquid obtained was then heated on the water-bath until all the pentachloride had dissolved, allowed to remain for five minutes, and then poured, with constant stirring, into 300 c.c. of light petroleum. The reddish-coloured precipitate was collected, washed with light petroleum, and dried in a desiccator:

0·1068 gave 0·2464 CO<sub>2</sub> and 0·0276 H<sub>2</sub>O. C=62·92; H=2·87.  
0·1002 „ 0·1210 AgCl. Cl=29·87.

C<sub>19</sub>H<sub>14</sub>OCl<sub>3</sub> requires C=63·07; H=3·04; Cl=29·49 per cent.

The xanthonium chloride is a reddish-yellow solid which decomposes at about 200°. It is insoluble in non-hydroxylic solvents, and is rapidly decomposed by hydroxylic solvents.



In the preparation of this substance, 3 grams of dichlorophenylxanthonium chloride were heated on the water-bath with 0·6 gram of potassium cyanide and 20 c.c. of alcohol. The precipitated solid was collected, washed, and recrystallised from hot alcohol:

0·1170 gave 0·2940 CO<sub>2</sub> and 0·0332 H<sub>2</sub>O. C=68·53; H=3·15.

0·1040 „ 0·0856 AgCl. Cl=20·36.

0·2654 „ 9 c.c. N<sub>2</sub> (dry) at 22° and 758 mm. N=3·91.

C<sub>22</sub>H<sub>11</sub>ONCl<sub>2</sub> requires C=68·15; H=3·12; Cl=20·17;

N=3·98 per cent.

The nitrile crystallises in minute, reddish-brown crystals, and is very sparingly soluble in hot alcohol or glacial acetic acid. It decomposes at 280°.

*3:6-Dichloro-9-phenylxanthen-9-carboxylic acid* was prepared by heating 10 grams of the nitrile with 150 c.c. of alcohol and 25 c.c. of

concentrated hydrochloric acid, under reflux, for two hours. On cooling, the acid separated as a microcrystalline powder. It was purified by dissolving in sodium carbonate, filtering the solution, and reprecipitating the acid with dilute hydrochloric acid, and, finally, recrystallised from alcohol:

0·1142 gave 0·2690 CO<sub>2</sub> and 0·0374 H<sub>2</sub>O. C=64·24; H=3·64.  
0·1020 „ 0·0806 AgCl. Cl=19·55.

C<sub>20</sub>H<sub>12</sub>O<sub>3</sub>Cl<sub>2</sub> requires C=64·69; H=3·23; Cl=19·13 per cent.

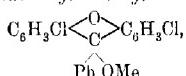
The free acid is a reddish-brown solid, which blackens when heated to about 300°. It is sparingly soluble in alcohol or acetic acid, and insoluble in hydrocarbon solvents. The *ethyl ester* was obtained by heating 1 gram of the acid with 5 grams of concentrated hydrochloric acid and 20 grams of alcohol under reflux for four hours. The solution was then poured out into sodium carbonate solution, and the precipitate collected, washed, and recrystallised from alcohol:

0·1076 gave 0·2616 CO<sub>2</sub> and 0·402 H<sub>2</sub>O. C=66·30; H=4·15.  
0·2340 „ 0·1680 AgCl. Cl=17·76.

C<sub>22</sub>H<sub>16</sub>O<sub>3</sub>Cl<sub>2</sub> requires C=66·17; H=4·01; Cl=17·80 per cent.

The ester is a reddish-brown powder, which is sparingly soluble in alcohol or pyridine. It decomposes at about 200°.

3:6-Dichloro-9-phenylxanthyl methyl ether,



was prepared by adding 2 grams of the dichloroxanthonium chloride to the calculated quantity of sodium methoxide, dissolved in 25 c.c. of methyl alcohol. The solution was heated under reflux for half an hour, and then poured into 50 c.c. of water, the whole being boiled, and finally acidified with dilute acid. The precipitate was collected, washed, dried, and recrystallised from alcohol:

0·1226 gave 0·3042 CO<sub>2</sub> and 0·0420 H<sub>2</sub>O. C=67·67; H=3·50.  
0·1590 „ 0·1308 AgCl. Cl=20·35.

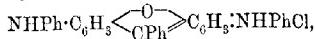
C<sub>20</sub>H<sub>14</sub>O<sub>2</sub>Cl<sub>2</sub> requires C=67·23; H=3·92; Cl=19·95 per cent.

The ether decomposes at about 220°, and is a reddish-brown powder, which is sparingly soluble in the ordinary organic solvents.

The *ethyl ether* was prepared in a similar manner, and shows the same characteristics:

0·1105 gave 0·2740 CO<sub>2</sub> and 0·410 H<sub>2</sub>O. C=67·63; H=4·12.  
0·1130 „ 0·090 AgCl. Cl=19·70.

C<sub>21</sub>H<sub>16</sub>O<sub>2</sub>Cl<sub>2</sub> requires C=67·94; H=4·31; Cl=19·13 per cent.

*Rosamine Derivatives.**3:6-Dianilino-9-phenylxanthenyl chloride,*

was obtained by heating 5 grams of dichlorophenylxanthonium chloride for five minutes with 25 c.c. of aniline. The resulting paste was then stirred into 200 c.c. of water, and the mixture rendered alkaline and distilled in steam to remove excess of aniline. The residual mixture was acidified, the precipitate collected, well washed, and recrystallised from alcohol:

0·1100 gave 0·3150 CO<sub>2</sub> and 0·0465 H<sub>2</sub>O. C=78·10; H=4·70.

0·2040 " 0·0600 AgCl. Cl=7·28.

0·3546 " 16·4 c.c. N<sub>2</sub> (dry) at 23° and 765 mm. N=5·33.  
C<sub>31</sub>H<sub>25</sub>ON<sub>2</sub>Cl requires C=78·39; H=4·84; Cl=7·48; N=5·31 per cent.

The rosamine chloride crystallises in small, bluish-purple needles, and is sparingly soluble in alcohol. Its solution possesses an intense green fluorescence.

*3:6-Di-o-toluidino-9-phenylxanthenyl chloride* is prepared in a similar manner from the dichloroxanthonium chloride and *o*-toluidine:

0·1002 gave 0·2982 CO<sub>2</sub> and 0·0488 H<sub>2</sub>O. C=81·17; H=5·40.

0·2066 " 0·584 AgCl. Cl=6·99.

0·350 " 16 c.c. N<sub>2</sub> (dry) at 22° and 765 mm. N=5·32.  
C<sub>31</sub>H<sub>27</sub>ON<sub>2</sub>Cl requires C=81·39; H=5·55; Cl=7·06; N=5·58 per cent.

It is a purple-red solid, which is somewhat soluble in alcohol, the solution showing an intense fluorescence.

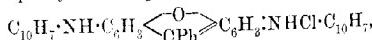
*3:6-Di-p-toluidino-9-phenylxanthenyl chloride* was prepared in a similar manner from *p*-toluidine:

0·1102 gave 0·3276 CO<sub>2</sub> and 0·0535 H<sub>2</sub>O. C=81·08; H=5·39.

0·200 " 0·0564 AgCl. Cl=6·98.

0·3450 " 16 c.c. N<sub>2</sub> (dry) at 22° and 765 mm. N=5·40.  
C<sub>31</sub>H<sub>27</sub>ON<sub>2</sub>Cl requires C=81·39; H=5·55; Cl=7·06; N=5·58 per cent.

It resembles the ortho-compound in properties, but is somewhat darker in shade.

*3:6-Di-β-naphthylamino-9-phenylxanthenyl chloride,*

was obtained by heating dichlorophenylxanthonium chloride with an excess of β-naphthylamine. The product was poured into water.

rendered alkaline, and distilled in a current of steam. The residue was acidified, collected, washed, dried, and recrystallised from alcohol. It is a blue, microcrystalline solid, which is sparingly soluble in alcohol. It yields blue solutions, which show a violet fluorescence. When heated, it decomposes at 235°:

0·1008 gave 0·3018 CO<sub>2</sub> and 0·0444 H<sub>2</sub>O. C=81·65; H=4·89.

0·1170, " 0·0280 AgCl. Cl=5·92.

0·230, " 10 c.c. N<sub>2</sub> (dry) at 22° and 761 mm. N=5·04.

C<sub>23</sub>H<sub>27</sub>ON<sub>2</sub>Cl requires C=81·46; H=4·70; Cl=6·18; N=4·88 per cent.

*3:6-Di-p-aminophenylamino-9-phenylxanthenyl chloride* was prepared in the form of its dihydrochloride by the condensation of *p*-phenylenediamine with dichlorophenylxanthonium chloride. The solution of the free base was evaporated to small bulk, and a large excess of concentrated hydrochloric acid added. The precipitated diamine hydrochloride was collected, the filtrate being concentrated and extracted with alcohol. The alcoholic solution was then evaporated, and the hydrochloride finally recrystallised from water:

0·090 gave 0·2246 CO<sub>2</sub> and 0·0398 H<sub>2</sub>O. C=68·06; H=4·91.

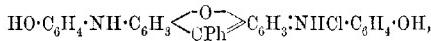
0·1230, " 0·0934 AgCl. Cl=18·78.

0·1825, " 15 c.c. N<sub>2</sub> (dry) at 22° and 760 mm. N=9·76.

C<sub>21</sub>H<sub>27</sub>ON<sub>4</sub>Cl<sub>3</sub> requires C=67·84; H=4·74; Cl=18·44; N=9·70 per cent.

The hydrochloride crystallises in minute, blue needles, and is very soluble in water or alcohol.

*3:6-Di-p-hydroxyphenylamino-9-phenylxanthenyl chloride*,



is similarly obtained from dichloroxanthonium chloride and *p*-aminophenol. The fusion is dissolved in ammonia, the solution filtered, and acidified by hydrochloric acid. It is then evaporated to dryness, extracted by alcohol, filtered, and again evaporated. The residue is dissolved in sodium hydroxide solution, and again precipitated by carbon dioxide. The precipitate is then collected, dissolved in alcoholic hydrochloric acid, the solution again evaporated, and the residue finally crystallised from dilute alcohol. In this way it is obtained in small, dark reddish-purple needles, which dissolve in the alkali hydroxides with a deep violet colour:

0·1172 gave 0·3034 CO<sub>2</sub> and 0·0508 H<sub>2</sub>O. C=70·60; H=4·82.

0·1040 lost 0·0035 H<sub>2</sub>O at 130°. H<sub>2</sub>O=3·36.

C<sub>21</sub>H<sub>23</sub>O<sub>3</sub>N<sub>2</sub>Cl<sub>3</sub>H<sub>2</sub>O requires C=70·92; H=4·77; H<sub>2</sub>O=3·43 per cent.

554 FUNK: SYNTHESIS OF DL-3:4-DIHYDROXYPHENYLALANINE

0·081\* gave 4 c.c. N<sub>2</sub> (dry) at 17° and 752 mm. N = 5·77.

0·1356\* „ 0·0376 AgCl. Cl = 6·86.

C<sub>31</sub>H<sub>28</sub>O<sub>3</sub>N<sub>2</sub>Cl requires N = 5·56; Cl = 7·01 per cent.

EAST LONDON COLLEGE,  
UNIVERSITY OF LONDON.

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LXV.—*Synthesis of dl-3:4-Dihydroxyphenylalanine.*

By CASIMIR FUNK.

THE question of the formation of adrenaline in the animal body has engaged much attention. The two amino-acids that suggest themselves as the parent substances of adrenaline are obviously tyrosine and phenylalanine, but certain considerations render it probable that the body is incapable of employing these substances for the formation of adrenaline. Thus, in cases of abnormal metabolism, tyrosine is eliminated as homogentisic acid (Wolkow and Baumann, *Zeitsch. physiol. Chem.*, 1891, **15**, 228; Falta and Langstein, *ibid.*, 1903, **37**, 513; Abderhalden, Bloch, and Rona, *ibid.*, 1907, **52**, 435), whilst no catechol derivatives have been obtained from any of the aromatic amino-acids.

In the experiments which have been conducted on this point, investigators have sought to bring about a transformation of tyrosine (Ewins and Laidlaw, *J. Physiol.*, 1910, **40**, 275) into adrenaline by incubating the former substance with suprarenal gland tissue. It may well be, however, that the formation of adrenaline takes place in several steps, and that different tissues of the body are necessary.

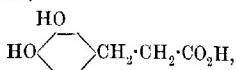
In order to be certain that adrenaline is really formed, it is necessary to find a chemical method by which this substance can be separated from amino acids, and such a separation is at present being attempted.

That some substance of the nature of tyrosine or phenylalanine is the precursor of adrenaline is further suggested by the fact that all three compounds belong to the same optical (*d*) series.

The synthesis of 3:4-dihydroxyphenylalanine has been effected with the idea that it may be the parent substance of adrenaline; experiments are also being conducted in order to ascertain whether any of this substance is contained in proteins. That this may be

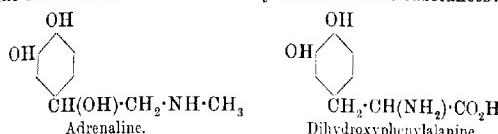
\* Anhydrous substance.

the case is indicated by the occurrence of caffeic acids in plants.  
A dihydroxycaffeic acid,



has been found by Lippmann in turnip leaves (*Ber.*, 1892, **25**, 3220).

A comparison of the formulæ of adrenaline and dihydroxyphenylalanine indicates a certain similarity between these substances:

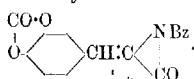


#### EXPERIMENTAL.

##### *Synthesis of 3:4-Dihydroxyphenylalanine.*

Dihydroxyphenylalanine was obtained according to the method described by Erlenmeyer and Halsey (*Annalen*, 1899, **307**, 138; *Ber.*, 1897, **30**, 2981) for the synthesis of tyrosine.

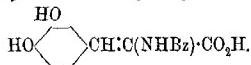
##### *Condensation of 3:4-Carbonyldioxybenzaldehyde and Hippuric Acid: Lactimide of $\alpha$ -Benzoylaminoo-3:4-dihydroxycinnamic Acid,*



Sixty grams of 3:4-carbonyldioxybenzaldehyde were mixed with 60.5 grams of hippuric acid and 30 grams of anhydrous sodium acetate, and the mixture was heated for one hour on the water-bath with 112 grams of acetic anhydride. The solution became yellow, and in a short time a yellow, crystalline substance separated out. Owing to the insolubility of this substance in the ordinary solvents, it was found necessary to purify it by boiling, first with water and then with alcohol. The crystals obtained in this way consisted of small, yellow plates, which melted about 238°. Yield = 83 grams, or 74 per cent. of the theoretical. After drying in a vacuum at 70°, the substance was analysed:

0.3116 gave 0.7604 CO<sub>2</sub> and 0.0906 H<sub>2</sub>O. C = 66.55; H = 3.23.  
0.4266, by Kjeldahl's method, required 13.5 c.c. N/10-H<sub>2</sub>SO<sub>4</sub>.  
N = 4.43.

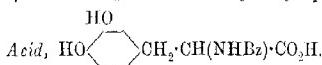
C<sub>17</sub>H<sub>14</sub>O<sub>5</sub>N requires C = 66.43; H = 2.95; N = 4.56 per cent.

*$\alpha$ -Benzoylamino-3:4-dihydroxycinnamic Acid,*

Eighty-three grams of the lactimide prepared as above were heated on the water-bath with 500 c.c. of 10 per cent. sodium hydroxide solution. In this way, both the lactimide and carbonyldioxy-groups were hydrolysed. After cooling and neutralising with hydrochloric acid, a resinous mass separated out, which became crystalline after keeping for some time in the cold. This was twice recrystallised from alcohol, when small, yellow plates were obtained, which, on drying in a vacuum, melted at 210—215°. At 100° it sublimed to form colourless plates. The yield was 60 grams, or 75 per cent. of the theoretical:

0.2268 gave 0.5368 CO<sub>2</sub> and 0.0902 H<sub>2</sub>O. C = 64.55; H = 4.31.  
0.39, by Kjeldahl's method, required 12.2 c.c. N/10-H<sub>2</sub>SO<sub>4</sub>.  
N = 4.35.

C<sub>16</sub>H<sub>13</sub>O<sub>5</sub>N requires C = 64.18; H = 4.38; N = 4.68 per cent.

*Preparation of dl- $\alpha$ -Benzoylamino-3:4-dihydroxy- $\beta$ -phenylpropionic*

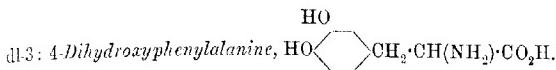
The 60 grams of the substance just described were suspended in 600 c.c. of water, and 750 grams of sodium amalgam added in small portions during forty-five minutes. The solution was neutralised with hydrochloric acid, and concentrated under diminished pressure in a stream of coal gas. Small, yellow, four-sided plates separated out. Yield, 19.6 grams, or 32 per cent. of the theoretical. By following the directions of E. Fischer (*Ber.* 1899, **32**, 3638), who, in his work on tyrosine, boiled the corresponding solution with 33 per cent. aqueous sodium hydroxide, all this substance seemed to be destroyed.

The crystals were recrystallised from water, and contained one molecule of water of crystallisation, which was expelled when heated in a vacuum at 110°. They are sparingly soluble in cold, and readily so in hot, water, also in alcohol, glacial acetic acid, or ethyl acetate, but not in benzene. The anhydrous substance melts at 190—195°:

1.092 lost 0.0596 H<sub>2</sub>O. H<sub>2</sub>O = 5.45.

C<sub>16</sub>H<sub>13</sub>O<sub>5</sub>N<sub>2</sub>H<sub>2</sub>O requires H<sub>2</sub>O = 5.64 per cent.  
0.2616 gave 0.614 CO<sub>2</sub> and 0.1132 H<sub>2</sub>O. C = 64.01; H = 4.80.

0·3248, by Kjeldahl's method, required 10·0 c.c. N/10-H<sub>2</sub>SO<sub>4</sub>. N=4·30.  
 C<sub>10</sub>H<sub>13</sub>O<sub>5</sub>N requires C=63·75; H=5·03; N=4·65 per cent.



18·2 Grams of the benzoyl compound were hydrolysed by boiling with sixty times its weight of 20 per cent. hydrochloric acid under a reflux condenser. The solution was left overnight in the cold, and the benzoic acid which separated out was collected. The filtrate was extracted with ether, and the aqueous solution concentrated in a vacuum. The residue obtained was dissolved in a small quantity of water, neutralised with ammonia, and concentrated under diminished pressure in an atmosphere of coal gas. On recrystallising from water, 5·7 grams of spindle-shaped crystals were obtained, corresponding with a yield of 47 per cent. of the theoretical. After being dried in a vacuum, the crystals melted at 263—272°:

0·21 gave 0·4218 CO<sub>2</sub> and 0·1042 H<sub>2</sub>O. C=54·75; H=5·51.  
 0·1838, by Kjeldahl's method, required 9·0 N/10-H<sub>2</sub>SO<sub>4</sub>. N=6·85.

C<sub>9</sub>H<sub>11</sub>O<sub>4</sub>N requires C=54·79; H=5·63; N=7·10 per cent.

This substance is readily oxidised in neutral, and more readily in alkaline, solution, with the formation of a black pigment. With nitric acid, a red coloration is obtained. Millon's reagent in the cold gives an orange colour, but on heating, reduction takes place. With ferric chloride, a green colour is formed, which, on boiling or on the addition of ammonia, becomes dark red. The substance reduces Fehling's solution on heating. It dissolves in water more easily than does tyrosine, and gives a crystalline hydrochloride, but an ethyl ester hydrochloride could not be obtained.

I am at present preparing the active *D*-compound and some derivatives of it, and intend shortly to publish some experiments on the physiological action of these compounds. I wish to express my thanks to Dr. Harden for granting me the use of his laboratory.

LISTER INSTITUTE OF PREVENTIVE MEDICINE,  
 CHELSEA, S.W.

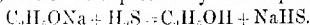
LXVI.—*The Action of Hydrogen Sulphide on the Alkyl oxides of the Metals. Part I. Sodium and Potassium Ethoxides.*

By ALEXANDER RULE.

THE work described in this paper forms the first portion of an investigation of certain metallic salts, which, owing to hydrolysis, cannot be obtained from aqueous solution, and up to the present have only been prepared in the dry way. The sulphides of chromium, aluminium, and ferric iron are examples of such compounds, and it is doubtful if these substances have ever been obtained in the pure state.

The possibility of preparing these sulphides from alcoholic solution by precipitation with either hydrogen sulphide or an alcoholic solution of sodium sulphide suggested itself to the author, but it was necessary, in the first place, to find derivatives of the metals which were soluble in alcohol, and which, on decomposition according to the method indicated, would not give rise to products likely to react in any way on the sulphides, if the latter were formed.

The alkyl oxides of the metals in question appeared to be suitable for trial in this way, but on endeavouring to ascertain if previous work had been done in this direction, the author was unable to find any record of the action of hydrogen sulphide, either on these compounds or on the alkyl oxides of sodium or potassium. The action of certain other gases, such as carbon monoxide, on the alkyl oxides of sodium and potassium is well known, and has been thoroughly investigated. When sodium is dissolved in absolute alcohol in such amount as to give a solution of sodium ethoxide of moderate concentration, and this solution is then saturated with dry hydrogen sulphide, no precipitate is formed, but on adding sufficient benzene or ether to the solution, a precipitate of practically pure anhydrous sodium hydrosulphide is obtained. A solution of potassium ethoxide, similarly treated, gives a precipitate of pure anhydrous potassium hydrosulphide. There is no indication of the formation of organic sulphur compounds, and from the results obtained under varied conditions, the reaction appears to be quantitative, and to be expressed by the simple equation:



In view of the considerable amount of work already done on the sulphides and hydrosulphides of the alkali metals, and the difficulty experienced in obtaining the anhydrous compounds in the pure

state, the investigation of this apparently simple method of preparation seemed of importance.

Gay Lussac and Thénard made an attempt to obtain the anhydrous hydrosulphides of sodium and potassium by the action of hydrogen sulphide on the heated metals. A brown mass was obtained, and to the sodium compound they ascribed the composition  $\text{Na}_3\text{HS}_2$ . According to Sabatier, these products always contain polysulphides.

Sabatier (*Ann. Chim. Phys.*, 1881, [v], **22**, 1) states that anhydrous sodium hydrosulphide is obtained by saturating crystals of sodium sulphide,  $\text{Na}_2\text{S}\cdot 9\text{H}_2\text{O}$ , with hydrogen sulphide, and evaporating the solution obtained in a current of hydrogen sulphide. The product is described as a yellowish-white mass, nearly pure. Bloxam (*Trans.*, 1900, **77**, 763) found, however, that sodium sulphide was only slowly acted on by hydrogen sulphide in the solid state, and failed to obtain sodium hydrosulphide by this method.

From the foregoing evidence it seems practically certain that the pure hydrosulphides are unobtainable by any of the methods mentioned. Bloxam (*loc. cit.*) describes a method suggested by Dr. Scott for the preparation of anhydrous potassium hydrosulphide. Hydrogen sulphide was passed into rectified ether containing metallic potassium, and in this way the hydrosulphide was obtained pure as a pale yellow, crystalline powder.

The use of alcohol as a solvent for sodium hydroxide in the ordinary method for the preparation of sodium monosulphide is described by Böttger (*Annalen*, 1884, **223**, 335), but the resulting product was hydrated, owing to the formation of water by the action of hydrogen sulphide on the sodium hydroxide in solution.

The author of the present paper has also investigated the action of hydrogen sulphide on the pure dry ethoxides of sodium and potassium. In each case reaction takes place in the cold, the sole products being alcohol and the hydrosulphides of the metals. There is no evidence of the formation of the monosulphides, as is the case when hydrogen sulphide is allowed to act on dry sodium hydroxide (Kircher, *Annalen*, 1839, **31**, 339).

The simple reaction whereby anhydrous sodium hydrosulphide is obtained in alcoholic solution will doubtless prove of considerable value in the preparation of organic sulphur compounds, where, ordinarily, crystalline sodium hydrosulphide is employed. In these cases the presence of water of hydration, and often of free sodium hydroxide in the salt, occasions loss through hydrolysis.

### EXPERIMENTAL.

For analysis of the hydrosulphides dealt with in this section, gravimetric methods were employed in every case. Owing to the extremely hygroscopic character of these substances, it was found necessary to carry out weighing operations with special care and rapidity. Sulphur was estimated by oxidation with concentrated bromine water, and precipitation as barium sulphate. Sodium and potassium were estimated as sulphates, but before the addition of sulphuric acid to the substances they were treated with bromine water. Otherwise, the violent evolution of hydrogen sulphide on adding acid is liable to cause loss.

The action of hydrogen sulphide on sodium ethoxide in alcoholic solution can be illustrated very rapidly on a small scale by dissolving 0·5 gram of metallic sodium in about 10 c.c. of ethyl alcohol in a test-tube, adding an equal volume of dry benzene, and then passing in the gas. The solution becomes warm, and after a short time a precipitate begins to separate out, becoming thicker as the passage of the gas is continued. When the solution is saturated with the gas, the product is rapidly collected, washed with a little ether, and then placed immediately in a dessicator and allowed to remain in a vacuum. The substance obtained by this method possesses a light buff tint, is extremely deliquescent, and when freshly prepared dissolves in hydrochloric acid to a clear solution with violent evolution of hydrogen sulphide.

A similar experiment with potassium ethoxide gives a product quite analogous to the sodium compound, but only very faintly buff-coloured.

If the solution, after collecting the precipitate, is treated with a further quantity of benzene, or, better, with dry ether, a considerable precipitate is obtained, which is identical in properties and composition to the first product. It was obvious that in order to obtain a maximum yield, careful regulation of the relative amounts of alcohol and precipitant would be necessary.

#### *Action of Hydrogen Sulphide on a Saturated Solution of Sodium Ethoxide.*

Two grams of sodium were added to 20 c.c. of absolute ethyl alcohol (freshly distilled over lime) in a small flask fitted to a reflux condenser. When sodium ethoxide began to separate out, more alcohol was added, until just sufficient was present to retain the product in solution at room temperature. Forty c.c. of alcohol were required. The flask was then furnished with a tightly-fitting

cork, through which passed a delivery tube and an exit tube with calcium chloride bulb attached. Hydrogen sulphide, washed by passing through water, and then dried over a long column of calcium chloride, was passed into the solution in a rapid stream, and after a few minutes a fine crystalline precipitate began to form in the solution, and increased with continued passage of the gas.

When the solution was saturated with hydrogen sulphide, the precipitate was collected as rapidly as possible, sprayed with absolute alcohol, and kept in a vacuum over calcium chloride. The substance thus obtained was buff-coloured. It weighed 0·25 gram. For analysis a larger quantity was prepared under precisely similar conditions:

0·2514 gave 0·3142  $\text{Na}_2\text{SO}_4$ . Na=40·48.

0·2611 " 1·0721  $\text{BaSO}_4$ . S=55·84.

$\text{NaHS}$  requires Na=41·07; S=57·14 per cent.

The product is slightly impure sodium hydrosulphide, and there is no indication that double compounds of sodium ethoxide and monosulphide are formed in the course of the reaction, as the precipitate does not dissolve on continued passage of the gas, but increases in amount (compare Bloxam, *loc. cit.* Preparation of sodium monosulphide). This substance was found to contain a trace of iron, which appears to be an impurity of metallic sodium, and probably causes the coloration of the substance.

The filtrate from the above product was quickly transferred to a dry flask, and 50 c.c. of pure dry ether were added. A pure white, crystalline precipitate was immediately formed. The flask was corked and kept in a desiccator until the precipitate had settled, and a further quantity of ether was added, this operation being repeated until the addition of ether produced only a slight turbidity in the supernatant liquid: 110 c.c. of ether were used. The product was collected, washed with dry ether, and kept in a vacuum for several hours. Further addition of ether to the filtrate only produced a faint cloud.

The substance was a pure white, granular powder:

0·1598 gave 0·2010  $\text{Na}_2\text{SO}_4$ . Na=40·74.

0·1795 " 0·7398  $\text{BaSO}_4$ . S=56·71.

$\text{NaHS}$  requires Na=41·07; S=57·14 per cent.

4·31 Grams were obtained; thus the total yield of sodium hydrosulphide from 2 grams of sodium =  $4\cdot31 + 0\cdot25 = 4\cdot56$ . Theory requires 4·86 grams. (A slight loss occurred through a little of the substance sticking to the sides of the flask; owing to its hygroscopic nature it was neglected.) The reaction, therefore, appears

to be quantitative, but the amount of ether required to precipitate the product completely is considerable. The ether is, however, very easily recoverable in the pure state.

The freshly prepared compound dissolved to a clear solution in hydrochloric acid, with vigorous evolution of hydrogen sulphide. After the substance had been kept for a few days, a solution so obtained was faintly opalescent, owing to separation of a trace of sulphur derived from products of slight oxidation. The substance is extremely soluble in water, and moderately so in alcohol. On allowing it to remain in the air for a few moments, a faint odour of hydrogen sulphide is noticeable. It deliquesces very rapidly, forming an almost colourless solution, from which colourless crystals separate out after a few days (compare Bloxam, *loc. cit.*).

*Action of Hydrogen Sulphide on Sodium Ethoxide Suspended in Benzene.*

For the preparation of larger quantities of sodium hydrosulphide it was found more convenient to carry out the reaction in presence of the precipitant. Ether is unsuitable for this purpose on account of its volatility, but good results were obtained with benzene.

One hundred c.c. of pure dry benzene were mixed with 10 grams of absolute alcohol in a flask fitted with a reflux condenser, the inner tube of which was ground to fit the mouth of the flask. Five grams of metallic sodium in small pieces were introduced into the mixture, which was then heated to boiling on the water-bath. As the reaction slowed, further quantities of alcohol were added until the sodium was completely dissolved. On allowing to cool, sodium ethoxide separated out as a gelatinous mass. Dry hydrogen sulphide was passed in, and reaction took place immediately with considerable evolution of heat and the formation of a fine crystalline precipitate of sodium hydrosulphide. The passage of the gas was continued until the precipitate had settled, and no further turbidity was produced in the supernatant liquid. The product was collected, washed with dry benzene, and finally with dry ether, which caused a slight precipitation in the filtrate. After remaining for one day in a vacuum, it weighed 11.92 grams. Theory requires 12.15 grams. Yield = 98.1 per cent.:

0.2720 gave 0.3386 Na<sub>2</sub>SO<sub>4</sub>. Na = 40.32.

0.2429 „ 0.9992 BaSO<sub>4</sub>. S = 56.49.

NaHS requires Na = 41.07; S = 57.14 per cent.

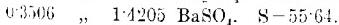
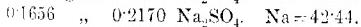
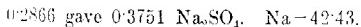
The substance was slightly buff-coloured, but in all other respects identical with that obtained by precipitation with ether. It was found somewhat difficult to remove the last traces of benzene from

the product, which still possessed a faint odour of the hydrocarbon after remaining in a vacuum for a week. It was finally expelled by heating the substance to 110° in a slow current of hydrogen.

*Action of Hydrogen Sulphide on Solid Sodium Ethoxide.*

One gram of metallic sodium was dissolved in absolute alcohol contained in a small distillation flask of known weight fitted to a condenser. Excess of alcohol was distilled off, and the product then heated gradually to 180° in an oil-bath, in a current of dry hydrogen, until no more alcohol passed over. Sodium ethoxide was obtained in this way as a perfectly homogeneous, white mass. The contents of the flask were then allowed to cool in hydrogen, and when quite cold, dry hydrogen sulphide was passed into the flask. The ethoxide immediately began to assume a light buff tint, which quickly spread over its surface. The mass became hot, alcohol was evolved, and condensed on the walls of the flask. After passage of the gas had continued for about twenty minutes, it was possible to detach a considerable portion of the substance from the glass by tapping the flask. The product was very light pink, and appeared homogeneous, except where it had been in contact with the glass; these portions were dirty white on the surface.

The substance was heated gradually to 90° in a current of hydrogen. Alcohol commenced to distil over, and continued up to 120°. At this temperature the escaping gas was tested, and found to contain traces of hydrogen sulphide, and in order to prevent possible decomposition of sodium hydrosulphide at higher temperatures, the heating was continued in a slow stream of hydrogen sulphide to 180°, during which the last traces of alcohol were driven over. The flask was then allowed to cool, tightly stoppered, and weighed. Weight of product = 2·41 grams. Theory requires 2·43 grams for 1 gram of sodium:



NaHS requires Na = 41·07; S = 57·14 per cent.

The substance dissolved in water, giving a faintly yellow and slightly cloudy solution. The small amount of impurity present appeared to be derived partly from the glass of the distillation flask, but the high figure obtained for sodium suggests that the reaction was not quite complete. The ease with which sodium ethoxide is acted on by moisture and carbon dioxide rendered it necessary to carry out all the operations in one vessel without admitting air, but it is then difficult to bring the substance into

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thorough contact with the current of gas, as it adheres closely to the walls of the flask.

The results obtained with potassium ethoxide agree with those for the sodium compound, the product being in every case anhydrous potassium hydrosulphide. The slight coloration present in some of the sodium hydrosulphide preparations was either much fainter or absent altogether in the case of the corresponding products obtained from metallic potassium. The figures obtained on analysis of these products suggest a rather higher degree of purity for ordinary commercial metallic potassium than for metallic sodium.

*Action of Hydrogen Sulphide on a Saturated Solution of Potassium Ethoxide.*

2·2 Grams of metallic potassium were dissolved in 15 c.c. of absolute ethyl alcohol, and dry hydrogen sulphide was passed in until the solution was saturated. The crystalline product which separated was collected, sprayed with absolute alcohol, and dried in a vacuum. Unlike the corresponding product obtained from sodium, it was pure white. When examined microscopically it was seen to consist of very minute, but well defined, cubes. Weight of product = 1·93 grams:

0·2382 gave 0·2872  $K_2SO_4$ . K=54·04.

KHS requires K=54·16 per cent.

The filtrate was treated with 75 c.c. anhydrous ether, and the white, crystalline precipitate collected, washed, and dried in a vacuum:

0·3763 gave 0·4534  $K_2SO_4$ . K=54·01.

0·2969 " 0·9561  $BaSO_4$ . S=44·22.

KHS requires K=54·17; S=44·44 per cent.

Total yield of potassium hydrosulphide = 3·91 grams. Theory requires 4·04 grams. The properties of the substance are similar to those of the sodium compound, but it appears to be even more hygroscopic.

*Action of Hydrogen Sulphide on Solid Potassium Ethoxide.*

This reaction was carried out exactly as in the case of the sodium compound. Reaction took place immediately in the cold, and was more vigorous than with sodium ethoxide. The flask became hot, and a considerable quantity of alcohol distilled over. The product remaining after all the alcohol had been driven off possessed a very faint buff tint, and appeared more homogeneous

than the corresponding sodium compound. It dissolved in water and hydrochloric acid, giving clear solutions:

0·2122 gave 0·2535  $K_2SO_4$ .  $K=53\cdot55$ .

0·1955 " 0·6196  $BaSO_4$ .  $S=43\cdot62$ .

KIIS requires  $K=54\cdot17$ ;  $S=44\cdot44$  per cent.

When the hydrosulphides are heated in the air they become yellow, and finally fuse to a dark red liquid. On cooling, a deep yellow solid is formed, which is soluble in water, giving a yellow solution, and is at once decomposed by hydrochloric acid, with vigorous evolution of hydrogen sulphide and precipitation of sulphur. Bloxam (*loc. cit.*) investigated the action of heat on potassium hydrosulphide, and determined its melting point, but there appear to be several matters in connexion with this action which require explanation, and further investigation is at present being carried out by the author.

The possibility of preparing the anhydrous monosulphides of sodium and potassium by the action of the hydrosulphides on the ethoxides in alcoholic solution, analogous to the ordinary preparation in aqueous solution, is obvious, and it is hoped to deal with this portion of the subject in a later paper.

In conclusion, I desire to thank Mr. J. Smeath Thomas, M.Sc., for kind assistance in connexion with this work.

INORGANIC LABORATORIES,  
UNIVERSITY OF LIVERPOOL.

### LXVII—*The Application of Viscometry to the Measurement of the Rate of Reaction.*

By ALBERT ERNEST DUNSTAN and ALBERT GEORGE MUSSELL.

SINCE the viscosity-coefficients of different substances vary between wide limits, it is possible to follow the course of a reaction, provided that there is sufficient variation in this property in the initial and final states. The application of physical methods to this end is already well known, and it will be sufficient briefly to notice the work of Patterson and McMillan in this direction. These authors (*Trans.*, 1907, **91**, 504; 1908, **93**, 1041) took advantage of the fact that the rotation of ethyl tartrate is eminently sensitive to the presence of foreign substances. It varies largely, for example, when ethyl tartrate is dissolved in different solvents; and, conversely,

when an isodynamically changing compound is dissolved in this active liquid, the rotation changes in sympathy. In accordance with this, the above-mentioned authors measured the velocities of isodynamic change for benzynaldoxime  $\rightarrow$  benzylaldoxime; piperonalynoxime  $\rightarrow$  piperonalantioxime;  $\omega$ -isonitrotoluene  $\rightarrow$   $\omega$ -nitrotoluene, and several similar cases. An important point brought out, which militates against the utility of this method for comparison purposes, is that the more highly purified ethyl tartrate afforded constants different from those given by the slightly less pure solvent, and, further, of course, the changing substance must be soluble in the ethyl tartrate.

The change of viscosity during a reaction has been used to follow the effect of heat on gelatin solutions (von Schroeder, *Zeitsch. physikal. Chem.*, 1903, **45**, 75). This author found  $d\eta/dt = K/(\eta_1 - \eta_2)$ , where  $\eta_2$  is the final value of the viscosity, so that if the total viscosity change be taken as a measure of the chemical change, it is obvious that a unimolecular reaction is here indicated. Beck, Trietsche, and Ebbinghaus (*Zeitsch. physikal. Chem.*, 1907, **58**, 425) also pointed out that change in viscosity might be utilised for the measurement of the velocity of a reaction.

In the present communication the authors have endeavoured to show that the viscometric method is applicable to a variety of chemical reactions, and probably to all, could the conditions be suitably governed. The following changes were found to be capable of measurement:

Freshly distilled acetoacetic ester (enolic)  $\rightarrow$  equilibrium mixture; aniline  $\rightarrow$  phenylthiocarbamide; ammonium thiocyanate  $\rightarrow$  thiocarbamide; ammonium cyanate  $\rightarrow$  carbamide; acetic anhydride  $\rightarrow$  acetic acid; benzoyl chloride  $\rightarrow$  benzoic acid; hydrolysis of benzynaldoxime.

(1) *The Change of Viscosity of Freshly Distilled Ethyl Acetoacetate.*

Schaum (*Ber.*, 1898, **31**, 1964) first showed that acetoacetic ester underwent a change of density on keeping. He made the following determinations:

Fresh distilled.	Density, after 6 hours.	Density, after 24 hours.
1·0278	1·0282	1·0282
1·0278	1·0284	1·0284
1·0265	1·0269	1·0270

A more complete study of this change has been carried out for us by Mr. Thole, with the following results.

The ester was purchased from Kahlbaum. It boiled at  $137^{\circ}$  240 mm. It was distilled at 6h. 25m. p.m.

Time h. m.	Density 25/4.	Viscosity.	$\alpha - x$ .	$\frac{1}{t} \cdot \log_e \frac{\alpha}{\alpha - x}$
6 36	1.02094	—	—	—
6 42	—	0.015330	0.000063	—
6 49	1.02119	0.015340	0.000053	0.0216
7 6	1.02123	—	—	—
7 9	—	0.015367	0.000026	0.0827
7 15	—	0.015376	0.000017	0.0395
7 23	1.02125	—	—	—
7 35	—	0.015385	0.000008	0.0389
7 42	1.02128	—	—	—
7 48	—	0.015393	—	—
8 2	1.02128	—	—	—
8 50	1.02128	—	—	—
Average.....				0.0339

The densities required for this calculation of the viscosity-coefficients are interpolated from the curve drawn through the experimental points.

Considering the very small differences, the values of  $\frac{1}{t} \cdot \log_e \frac{\alpha}{\alpha - x}$  are surprisingly constant.

### (2) Aniline Heated with Ammonium Thiocyanate to Form Phenylthiocarbamide.

A hot saturated solution of ammonium thiocyanate was made in aniline. This was filtered into the viscometer heated to 130° in an oil-bath. Many experimental difficulties were met with, notably in the streams of bubbles evolved, which choked the capillary. The crude phenylthiocarbamide which separated on treating the reaction mixture with dilute hydrochloric acid melted at 149°.

Time (mins.).	Time of flow.	$\alpha - x$ .	$\frac{1}{t} \cdot \log_e \frac{\alpha}{\alpha - x}$
0	177.2	—	—
4	171.2	5.8	0.177
7	168.6	3.2	0.186
11	167.0	1.6	0.161
15	165.6	0.2	0.211
19	165.4	—	—
Average.....			0.184

The probable cause of the reaction is the formation of thiocarbamide, which reacts with the large excess of aniline present to yield the phenyl derivative. In each case a unimolecular constant should be given.

### (3) Rate of Change of Ammonium Thiocyanate to Thiocarbamide.

Attempts were made at first to follow this reaction by allowing the melted thiocyanate to remain for several hours in the viscometer, immersed in an oil-bath, the temperature of which was kept constant at about 160°. Insuperable difficulties were met with, however,

in the streams of bubbles which passed up through the capillary. Better results were obtained when the ammonium thiocyanate was heated in an oil-bath in a corked flask at a constant temperature. Samples were withdrawn every stated interval, and as they solidified immediately, it would be taken as certain that the reaction terminated at the time of removal of the sample.

One gram of the sample was dissolved in 12 c.c. of water, and the viscosity determined immediately after filtration into the viscometer.

Temperature of oil-bath 160°. One gram of product dissolved in 12 c.c. of water.

Time of withdrawal (in hours).	Time of flow (in seconds).
0	230·0
1	231·5
2	233·0
4	235·0
7	236·0
11·5	236·1*
Pure thiocarbamide.....	248·0
Thiocarbamide heated 1 hour .....	240·0
" " 3½ hours ...	236·0

\* Part of product was insoluble, and odour of hydrogen sulphide was observed.

When these results are plotted, it is found that they lie on two curves which approach each other. The viscosity at equilibrium is 236, and this corresponds with an equilibrium mixture of 33 per cent. of thiocarbamide.

Polarimetrically, Patterson and McMillan (*loc. cit.*) obtain 45 per cent., whilst Werner and Reynolds (*Trans.*, 1903, **83**, 1) found 24·72 per cent. (at temperatures between 170° and 180°).

#### (4) Rate of Change of Ammonium Cyanate into Carbamide.

Very many experiments have been made on the measurement of this reaction. It has been found best to mix two cold equivalent saturated solutions of ammonium sulphate and potassium cyanate, filter off the precipitated potassium sulphate, and, on cooling further to filter the solution of ammonium cyanate into the viscometer. At the ordinary temperature (25°) the reaction proceeds slowly, yet measurably. A typical series is given below.

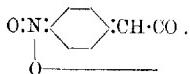
*Solution made at 9.40 a.m.*

Time (mins.).	Time of observation.	Time of flow.	$a - x$ .	$\frac{1}{t} \cdot \log_{10} \frac{a}{a - x}$
0	Wednesday 10.10 a.m.	4'29"	36.0	—
50	" 11.0 "	4'30"	35.0	0.00024
129	" 12.10 p.m.	4'32"	33.0	0.00031
238	" 2.8 "	4'34'6"	30.4	0.00031
247	" 2.17 "	4'35'0"	30.0	0.00032
290	" 3.0 "	4'36'0"	29.0	0.00032
350	" 4.0 "	4'38'0"	26.7	0.00037
560	" 7.30 "	4'45'0"	20.0	0.00045
Following Saturday...	12.30 "	5'5'0"	—	—

These values for  $K$  sufficiently confirm the experimental work of Patterson (*loc. cit.*), Walker, Hambly, Kay, and Wood (Trans., 1895, 67, 746; 1897, 71, 489; 1898, 73, 21) that this reaction is not of the first order.

(5) *Effect of Alkali on p-Nitrophenylacetonitrile.*

We are indebted to Mr. F. G. Pope, of East London College, for a supply of the above compound. On being dissolved in absolute alcohol, it gives a colourless solution, which, with a little alcoholic potassium hydroxide, turns to red. After several hours it darkens considerably, and on pouring into water, becomes emerald-green. It is possible that hydrolysis of the nitrile group goes on, followed by intramolecular change to a substance of the formula:



A saturated solution was made in ethyl alcohol, to which was added a few drops of alcoholic sodium hydroxide. The times of flow were plotted against times of observation, and a regular curve drawn through. The following results were obtained from interpolated values:

Time (mins.).	$a - x$ (in $\frac{1}{2}$ seconds).	$\frac{1}{t} \cdot \log_{10} \frac{a}{a - x}$
0	63	—
5	41	0.0373
10	32	0.0294
15	25	0.0267
20	18	0.0272
25	15	0.0249
30	11	0.0252
35	9	0.0241
40	6	0.0255
Average.....		0.0288

The reaction apparently tends to the first order after the first ten minutes.

(6) *The Hydration of Acetic Anhydride in Acetic Acid Solution.*

Many preliminary experiments have been carried out with the intention of studying the rate of hydration of acetic anhydride with the equivalent weight of water, both dissolved in pure acetic acid. As we are still working on this reaction, one set only will be here quoted.

5 c.c. acetic acid (frozen out repeatedly).  
4·72 c.c. acetic anhydride (b. p. 135°/739 mm.). 0·90 c.c. of water.

Time (mins.).	Time of flow (secs.).	$a - x$	$\frac{1}{t} \cdot \log_{10} \frac{a}{a - x}$
0	158·0	6·6	—
15	159·0	5·6	0·0048
22	159·6	5·0	0·0054
37	160·4	4·2	0·0053
45	161·2	3·4	0·0061
52	161·4	3·2	0·0060
65	164·0	2·6	0·0062
115	164·6	—	—
Average .....			0·00568

Our experiments indicate that the above reaction is by no means so simple as might be supposed, for at some concentrations the velocities of efflux become less as time goes on, whilst the absolute viscosities may rise to a maximum, and then steadily fall. This is shown in the accompanying table.

5 c.c. of acetic acid.  
4·72 c.c. of acetic anhydride. 0·45 c.c. of water.

Time.	Viscosity.	Time.	Viscosity.
12.22 p.m.	0·01379	4.32 p.m.	0·01370
12.31 "	0·01374	6.26 "	0·01368
12.44 "	0·01377	7.8 "	0·01365
12.57 "	0·01383	7.54 "	0·01362
3.12 "	0·01395	9.5 "	0·01359
4.14 "	0·01396	9.35 "	0·01352

(7) *The Hydrolysis of Benzoyl Chloride in Aqueous Acetone.*

Benzoyl chloride being not sufficiently soluble in water, a solution in aqueous acetone was made up of the following molecular concentrations: acetone, 100; water, 203·4; benzoyl chloride, 5·2.

Time (mins.).	Time of flow.	$\frac{1}{t} \cdot \log_{10} \frac{a}{a - x}$
11·5	406·2	—
14·5	412·2	0·00952
22·5	425·4	0·01025
44·5	441·0	0·00954
53·0	444·2	0·00956
80·0	448·0	0·01030
140·0	449·0	—
Average.....		0·00953

*Interpolated from curve:*

19.3	—	0.00854
34.0	—	0.00954
64.0	—	0.00956

The benzoyl chloride was recovered in the form of benzoic acid at the end of the experiment.

We have also made a number of experiments with the *syn*-oximes. We hoped to follow the transformation of these substances into their *anti*-isomerides, but up to the present have found no means of inducing the change. Benzynaldoxime, for example, is a very stable compound. It can be crystallised unchanged from hot alcohol, benzene, or amyl acetate, or even from hot water, so that our expectation that it would be converted into the *anti*-aldoxime in solution was not realised.

In conclusion, we wish to thank Mr. A. S. Wood and Mr. A. Perry for their assistance with the experiments on the oximes and benzoyl chloride respectively.

PHYSICAL CHEMICAL LABORATORY,  
EAST HAM TECHNICAL COLLEGE.

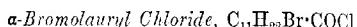
### LXVIII.—*Synthesis of Dipeptides of $\alpha$ -Aminolauric Acid with Glycine, Alanine, Valine, Leucine, and Asparagine.*

By ARTHUR HOPWOOD and CHARLES WEIZMANN.

In view of the possible presence of peptides of  $\alpha$ -aminolauric acid with amino-acids in the products of hydrolysis occurring in certain plants, the authors have prepared the dipeptides of  $\alpha$ -aminolauric acid with glycine and other amino-acids, so that they may be compared with the products obtained by the hydrolysis of proteins contained in *Laurus nobilis*, pichurum beans, and other proteins. From another point of view the peptides derived from higher fatty acids are of considerable interest, since a study of their properties may throw some light on the lipoproteins and the transformation of proteins proper into lipoproteins, a process probably taking place in the fatty degeneration of the cell (Bondi and Frankl, *Biochem. Zeitsch.*, 1909, **17**, 543).

## EXPERIMENTAL.

The method of synthesis adopted was one which has been successfully used by Emil Fischer (*Ber.*, 1903, **36**, 2982 *et seq.*) in the synthesis of polypeptides containing the radicles of the lower members of the series of fatty acids. In brief, the method consists in condensing  $\alpha$ -bromolauryl chloride with amino-acids in presence of sodium hydroxide, and then displacing the halogen in the product by an amino-group through the action of ammonia.



One hundred grams of phosphorus pentachloride (1 mol.) are added gradually, with vigorous shaking, to 134 grams of  $\alpha$ -bromo lauric acid (1 mol.), and, after the energetic action has subsided, the mixture is heated on a water-bath for an hour. The product is distilled under diminished pressure, and the fraction boiling at  $150-175^\circ/16$  mm. is collected. Yield, 95 grams:

0·3010 gave  $\text{AgCl} + \text{AgBr} = 0\cdot3380$ .

$\text{C}_{12}\text{H}_{22}\text{OBrCl}$  requires  $\text{AgCl} + \text{AgBr} = 0\cdot3351$  per cent.

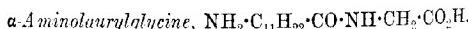
$\alpha$ -Bromolauryl chloride is a colourless liquid, which boils at  $150-10$  mm., and at  $170^\circ/16$  mm. It has a pungent odour, and is decomposed slowly by water.



Forty grams of  $\alpha$ -bromolauryl chloride (1 mol.) and an aqueous solution containing 5 grams of sodium hydroxide (1 mol.) are added gradually and alternately, with frequent shaking, to an aqueous solution containing 10 grams of glycine (1 mol.) and 5 grams of sodium hydroxide (1 mol.). The solution is heated on a water-bath until the odour of  $\alpha$ -bromolauryl chloride disappears, then allowed to cool, and dilute hydrochloric acid added in slight excess. A colourless precipitate of impure  $\alpha$ -bromolaurylglycine separates out, which is allowed to remain for several hours, then collected, washed with cold water, and dried in air on a porous plate. Yield, 43 grams. The product crystallises from benzene in colourless, rhombic plates, which melt at  $117-118^\circ$ . The crystals are only sparingly soluble in water, but readily so in alcohol, ether, benzene, toluene, or alkalis:

0·1627 gave 0·0921  $\text{AgBr}$ .  $\text{Br} = 24\cdot09$ .

$\text{C}_{14}\text{H}_{26}\text{O}_3\text{NBr}$  requires  $\text{Br} = 23\cdot78$  per cent.



Five grams of  $\alpha$ -bromolaurylglycine are mixed with excess of strong aqueous ammonia, and the mixture heated at  $100^\circ$  for an

hour. On evaporating the solution until the excess of ammonia is expelled, colourless crystals are obtained, from which water is removed by adding absolute alcohol, and then evaporating to dryness on a water-bath. In order to remove the ammonium bromide and unchanged  $\alpha$ -bromolaurylglycine, the dry residue is boiled with absolute alcohol, and then collected, when 3 grams of nearly pure  $\alpha$ -aminolaurylglycine are obtained. For further purification, the dipeptide is dissolved in absolute alcohol containing a little aqueous ammonia, filtered, and the filtrate boiled until the ammonia disappears, when the pure peptide separates out, and is collected, washed with absolute alcohol, and dried in air on a porous plate. It forms prismatic needles, which sinter at 207°, and melt and decompose at 214—214.5°:

$\text{C}_10\text{H}_{17}\text{O}_2$  gave 0.4475 CO<sub>2</sub> and 0.1858 H<sub>2</sub>O. C=61.79; H=10.52.

$\text{C}_10\text{H}_{17}\text{O}_2$  at 19.0° and 757.6 mm. N=10.58.

$\text{C}_{14}\text{H}_{25}\text{O}_3\text{N}_2$  requires C=61.70; H=10.36; N=10.29 per cent.

The dipeptide is almost insoluble in water, sparingly soluble in alcohol, but readily so in ammonia, alkali hydroxides, or mineral acids. When dissolved in dilute sulphuric acid, it gives a white, amorphous precipitate with aqueous phosphotungstic acid, which, as in the case of the proteins, is soluble in excess of the reagent. In presence of alkali hydroxide, the dipeptide condenses with  $\beta$ -naphthalenesulphonyl chloride, yielding  $\beta$ -naphthalenesulphonyl- $\alpha$ -aminolaurylglycine, which crystallises from much water in colourless, rhombic plates, melting and decomposing at 205—207°.

*$\alpha$ -Bromolaurylalanine*,  $\text{C}_{11}\text{H}_{22}\text{Br}\cdot\text{CO}\cdot\text{NH}\cdot\text{CHMe}\cdot\text{CO}_2\text{H}$ .

Ten grams of  $\alpha$ -bromolauryl chloride (1 mol.) and 34 c.c. of *N*-sodium hydroxide (1 mol.) are added gradually and alternately, with frequent shaking, to a solution containing 3 grams of alanine (1 mol.) in 34 c.c. of *N*-sodium hydroxide (1 mol.). The solution is heated on a water-bath until the odour of  $\alpha$ -bromolauryl chloride disappears, then allowed to cool, and dilute hydrochloric acid added in slight excess. A curdy, colourless precipitate of impure  $\alpha$ -bromolaurylalanine separates out, which is kept for several days, then collected, washed with water, and dried. Yield, 9.6 grams. The product crystallises from benzene in colourless, rhombic plates, which melt very sluggishly at 104—116°, probably indicating a mixture of two stereoisomeric  $\alpha$ -bromolaurylalanines. The crystals are sparingly soluble in hot water, moderately so in dilute alcohol, and readily so in absolute alcohol, ether, benzene, toluene, or alkalies:

$\text{C}_{11}\text{H}_{22}\text{Br}\cdot\text{CO}\cdot\text{NH}\cdot\text{CHMe}\cdot\text{CO}_2\text{H}$  gave 0.0670 AgBr. Br=23.15.

$\text{C}_{11}\text{H}_{22}\text{Br}\cdot\text{CO}\cdot\text{NH}\cdot\text{CHMe}\cdot\text{CO}_2\text{H}$  requires Br=22.82 per cent.

*α-Aminolaurylalanine*,  $\text{NH}_2\text{C}_{11}\text{H}_{22}\text{CO}\cdot\text{NH}\cdot\text{CHMe}\cdot\text{CO}_2\text{H}$

Five grams of *α*-bromolaurylalanine, when treated with aqueous ammonia in the same way as *α*-bromolaurylglycine, yield 2·9 grams of *α*-aminolaurylalanine, which crystallises from alcohol in prismatic needles, melting and decomposing at 212–213°. The dipeptide is sparingly soluble in water, moderately so in alcohol, and readily so in ammonia, alkali hydroxides, or mineral acids. A white, amorphous precipitate is produced when an aqueous solution of phosphotungstic acid is added to a solution of the dipeptide in dilute sulphuric acid:

0·1518 gave 0·3493  $\text{CO}_2$  and 0·1451  $\text{H}_2\text{O}$ . C = 62·75; H = 10·09.  
0·1173 „ 9·9 c.c.  $\text{N}_2$  at 18·0° and 769·3 mm. N = 10·02.  
 $\text{C}_{15}\text{H}_{30}\text{O}_3\text{N}_2$  requires C = 62·88; H = 10·56; N = 9·79 per cent.

*α-Bromolaurylvaline*,  $\text{C}_{11}\text{H}_{22}\text{Br}\cdot\text{CO}\cdot\text{NH}\cdot\text{CH}(\text{CO}_2\text{H})\cdot\text{CHMe}_2$

Ten grams of *α*-bromolauryl chloride are condensed, as described for *α*-bromolaurylalanine, with 4 grams of valine. The yield of impure *α*-bromolaurylvaline is 9·0 grams. The product crystallises from benzene in small, rhombic plates, which melt at 137–140°. The crystals are sparingly soluble in hot water, readily so in dilute or absolute alcohol, ether, benzene, toluene, or alkalies:

0·2484 gave 0·1214 AgBr. Br = 20·80.

$\text{C}_{17}\text{H}_{32}\text{O}_3\text{NBr}$  requires Br = 21·13 per cent.

*α-Aminolaurylvaline*,  $\text{NH}_2\text{C}_{11}\text{H}_{22}\text{CO}\cdot\text{NH}\cdot\text{CH}(\text{CO}_2\text{H})\cdot\text{CHMe}_2$

Five grams of *α*-bromolaurylvaline, when treated with aqueous ammonia in the same way as *α*-bromolaurylglycine, yield 3·5 grams of *α*-aminolaurylvaline, which crystallises from alcohol in small rhombic plates, sintering at 205°, and melting and decomposing at 212–214°. The dipeptide is almost insoluble in water, sparingly soluble in alcohol, and readily so in ammonia, alkali hydroxides, or mineral acids. A white, amorphous precipitate is produced when an aqueous solution of phosphotungstic acid is added to a solution of the dipeptide in dilute sulphuric acid:

0·1185 gave 0·2818  $\text{CO}_2$  and 0·1162  $\text{H}_2\text{O}$ . C = 64·83; H = 10·97.  
0·1236 „ 9·6 c.c.  $\text{N}_2$  at 18·5° and 772·3 mm. N = 9·24.  
 $\text{C}_{15}\text{H}_{34}\text{O}_3\text{N}_2$  requires C = 61·91; H = 10·90; N = 8·92 per cent.

*α-Bromolauryl leucine*,  $\text{C}_{11}\text{H}_{22}\text{Br}\cdot\text{CO}\cdot\text{NH}\cdot\text{CH}(\text{CO}_2\text{H})\cdot\text{CH}_2\text{CHMe}_2$

Ten grams of *α*-bromolauryl chloride are condensed, as described for *α*-bromolaurylalanine, with 4·4 grams of *r*-leucine. The yield

of impure  $\alpha$ -bromolauryl-leucine is 10·5 grams. The product crystallises from dilute alcohol in large, colourless, prismatic plates, and from benzene in colourless, rhombic plates, melting at 128–131°. The crystals are sparingly soluble in water, moderately so in dilute alcohol, and readily so in absolute alcohol, acetone, ethyl acetate, benzene, or alkalis:

0·1018 gave 0·0493 AgBr. Br=20·61.

$C_{18}H_{34}O_3NBr$  requires Br=20·37 per cent.

$\alpha$ -aminolauryl-leucine,  $NH_2 \cdot C_{11}H_{22} \cdot CO \cdot NH \cdot CH(CO_2H) \cdot CH_2 \cdot CHMe_2$ .

Five grams of  $\alpha$ -bromolauryl-leucine, when treated with aqueous ammonia in the same way as  $\alpha$ -bromolaurylglycine, yield 3·0 grams of  $\alpha$ -aminolauryl-leucine, which crystallises from alcohol in stout prisms melting and decomposing at 223·5–225·5°. The dipeptide is sparingly soluble in water, moderately so in alcohol, and readily so in ammonia, alkali hydroxides, or mineral acids. A white, amorphous precipitate is produced when an aqueous solution of phosphotungstic acid is added to a solution of the dipeptide in dilute sulphuric acid:

0·1018 gave 0·2465  $CO_2$  and 0·1014  $H_2O$ . C=66·04; H=11·14.

0·2344 „ 16·7 c.c.  $N_2$  at 19·5° and 768·1 mm. N=8·41.

$C_{18}H_{36}O_3N_2$  requires C=65·80; H=11·05; N=8·53 per cent.

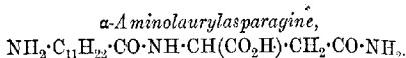
$\alpha$ -Bromolauryl-asparagine,  
 $C_{11}H_{22}Br \cdot CO \cdot NH \cdot CH(CO_2H) \cdot CH_2 \cdot CO \cdot NH_2$ .

Five grams of  $\beta$ -asparagine (1 mol.) are dissolved in 33·5 c.c. of  $N$ -sodium hydroxide (1 mol.), and then a further quantity of 33·5 c.c. of  $N$ -sodium hydroxide (1 mol.) and 9·92 grams of  $\alpha$ -bromolauryl chloride are added gradually and alternately with vigorous shaking. The temperature is kept at about 15° by cold water. On adding a slight excess of dilute hydrochloric acid to the clear solution, a pale yellow precipitate of impure  $\alpha$ -bromolaurylasparagine separates out, which is collected, washed with water, and dried. Yield, 12 grams. On crystallising the product from absolute alcohol, a mixture of colourless, rhombic plates and long, prismatic needles is obtained; these melt and decompose at 148–150°. The crystals are only sparingly soluble in water or benzene, but readily so in dilute or absolute alcohol, ammonia, or alkali hydroxides:

0·1889 gave 11·6 c.c.  $N_2$  at 19·5° and 779·2 mm. N=7·35.

0·1650 „ 0·0786 AgBr. Br=20·27.

$C_{16}H_{29}O_4N_2Br$  requires N=7·13; Br=20·32 per cent.



Five grams of  $\alpha$ -bromolaurylasparagine, when treated with aqueous ammonia in the same way as  $\alpha$ -bromolaurylglycine, yield 2·5 grams of  $\alpha$ -aminolaurylasparagine, which crystallises from absolute alcohol in colourless, rhombic plates, melting and decomposing at 242·0—243·5°. The dipeptide is sparingly soluble in water or alcohol, but readily so in ammonia, alkali hydroxides, or mineral acids. A white, amorphous precipitate is produced when an aqueous solution of phosphotungstic acid is added to a solution of the dipeptide in dilute sulphuric acid:

0·1135 gave 0·2415 CO<sub>2</sub> and 0·0970 H<sub>2</sub>O. C=58·02; H=9·56.  
 0·1206 „ 13·0 c.c. N<sub>2</sub> at 18·0° and 778·2 mm. N=12·95.  
 $\text{C}_{16}\text{H}_{31}\text{O}_4\text{N}_3$  requires C=58·30; H=9·49; N=12·77 per cent.

*Action of Enzymes on the Dipeptides.*

Pancreatic juice activated by kinase, pancreatin (Defresne), trypsin (Merck), muscle juice, or liver extract hydrolyse  $\alpha$ -aminolaurylglycine, but papayotin (Merck) is without action.

Micro-organisms develop slowly on ordinary artificial media containing  $\alpha$ -aminolaurylglycine as the sole source of nitrogen. The feeble growth of micro-organisms can be ascribed to the sparing solubility of the peptides in aqueous solutions of the media. If *B. Subtilis*, *B. Pyocyanus*, or *Proteus vulgaris* are cultivated on dilute solutions of peptone rendered slightly alkaline with potassium carbonate and saturated with  $\alpha$ -aminolaurylglycine, a decomposition of the peptide is observed after twenty-four hours.

In carrying out these biological tests, considerable assistance was afforded us by Dr. Berthelot, of the Pasteur Institute.

THE UNIVERSITY,  
 MANCHESTER.

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